PALLIATIVE CARE
IN THE
DEVELOPING WORLD
PRINCIPLES AND PRACTICE



Edited by Eduardo Burera, MD; Liliana De Lima, MHA; Roberto Wenk, MD and William Farr, MD

First Edition

PALLIATIVE CARE IN DEVELOPING COUNTRIES: PRINCIPLES AND PRACTICE

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FOREWORD FOR IAHPC PUBLICATION

We live in a world divided into those who have and those who have not; a world where the 'developed' countries can offer sophisticated medical care whilst the 'developing ' countries have to cope, not only with scarcity of essential resources, but also with famine, poverty, ignorance and immature governments. Death is still often regarded as a medical failure, and dying a time of inevitable suffering which few doctors and nurses have been trained to relieve

However, depressing as all this sounds, there is something to celebrate - the advent and worldwide development of Palliative Care - the response to those who claim "there is nothing more we can do." Palliative Care proclaims that suffering, even the suffering of the dying, can be relieved without expensive sophisticated technology.

Palliative Care is appropriate for every patient we are ever asked to help, whatever their illness, whatever its stage, wherever they live, whatever their colour, creed or class, whether they are rich or poor. Palliative care proclaims to the world - developed and developing – that dying need not be associated with unrelieved pain, and that bringing comfort to patients is within the power of each one of us, wherever we are. Here, in this small but packed book, the knowledge about how to do that is brought to us by colleagues from around the world.

Palliative Care started in a developed country but must, as a matter of urgency, cross all Man-made barriers and become available to all who need it. That is the mission of the International Association for Hospice and Palliative Care (IAHPC) which has produced and now offers this book to the developing world, and with it all the experience, expertise and best wishes of its hundreds of members worldwide.

Nothing more we can do? There is always more we can do if we employ the principles set out in this book which I enthusiastically commend to you.

Derek Doyle, OBE, MD, FRCSE, FRCPE, FRCGP
Edinburgh, Scotland

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PREFACE

The modern palliative care movement was originally developed in the United Kingdom in the 1960s as a response to the unmet needs of patients and their families as they confront a complex of problems that occur at the end of life. Initially a British movement, it soon became global.

A large body of knowledge has emerged about the assessment and management of the physical and psychosocial problems that occur in patients who develop cancer and other progressive, incurable illnesses. However, the overwhelming majority of the written literature describes the delivery of palliative care for diseases that occur mostly in the developed world and using treatment resources mostly available in such regions.

Patients in developing countries die younger and of different conditions compared to those in the developed world. In addition, socioeconomic and cultural issues make the management of these patients and the support of their families very different. Unfortunately, there is very limited information on the principles and practice of palliative care in these countries.

The developing world is far from being a homogenous area. There are a limited number of excellent facilities that have the latest technology and medications capable of providing care similar to that found in developed countries, but only to a few patients who can afford it. The majority of the population does not have access to these institutions; consequently they are cared for in facilities with limited resources. The chapters of this book provide information about specific conditions for health care professionals and palliative care teams working in these settings as well as the epidemiology of mortality, socioeconomic and cultural issues, and some practical aspects of community-based care in the developing world.

We identified contributors who combine strong academic and clinical experience, and in some cases, invited a team of two or more authors to provide comprehensive coverage of less common problems. Because of the wide difference in contributions, we found it impossible to adopt a uniform structure for all chapters, and worked with each author to obtain the most appropriate format for the very diverse subjects.

The purpose of this book is to provide health care professionals information on palliative care delivery for specific conditions that are prevalent in the developing world, as well as the special challenges that progressive conditions pose when they occur in countries with limited resources. It is intended to assist in the clinical delivery of care to patients and families, rather than as a scholarly volume. We have therefore minimized the number of references and tried to keep all chapters short and simple with the purpose of facilitating reading and minimizing cost.

This book should be useful to physicians, nurses, and other health care professionals delivering care in developing countries and to health care professionals in developed countries who are planning educational activities in the developing world.

We are grateful with all the contributors for their generous and timely efforts, and the International Association of Hospice and Palliative Care (IAHPC) for its funding and logistic support and hope that this book will lead to improved care at the end of life for patients and their families living in developing countries.

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Liliana De Lima, MHA
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William Farr, MD, PhD

1 Palliative Care: Basic Principles

Roger Woodruff, MD, MBBS, FRACP, FRAChPM

> Death should simply become
> a discrete but dignified exit
> of a peaceful person
> from a helpful society …
> without pain or suffering
> and ultimately without fear
>
> *Philippe Aries, 1977*
> *The Hour of Our Death*

WHAT IS PALLIATIVE CARE?

There is no one entirely satisfactory definition of palliative care. A simple and useful definition, modified from one developed by Derek Doyle and his colleagues, is

> Palliative care is the care of patients with progressive, far-advanced disease and a short life expectancy, for whom the focus of care is the relief and prevention of suffering and the quality of life.

This definition focuses on the quality of whatever life remains for the patient. It is person-orientated not disease-orientated. It is not primarily concerned with either life prolongation (or with life shortening) or with producing long-term disease remission. It is holistic in approach and aims to address all the patient's problems, both physical and psychosocial. A multi-disciplinary approach involving doctors, nurses and allied health professionals is employed to cover all aspects of care. The message of palliative care is that whatever the disease, however advanced it is, whatever treatments have already been given, there is always something that can be done to improve the quality of the life remaining to the patient.

The definition does not mention the site of care, for the principles of palliative care are the same whether the patient is at home or in a hospital or hospice. The terms dying and terminal care are not used because the principles and practices of palliative care should be employed long before the final days or weeks of life; terminal care and care of the dying are two stages of the continuum of palliative care.

The World Health Organization (WHO) definition of palliative care is shown in Table 1.

PALLIATIVE CARE AND SUFFERING

Suffering may be defined as the distress associated with events that threaten the intactness or wholeness of the person. In clinical practice, it is helpful to have a simple classification of suffering so that the complex problems presented by patients may be disentangled, in order to provide comprehensive palliation and relief of suffering. The causes of suffering may be grouped by their

physical, psychological, social, cultural or spiritual origin (Figure 1). For patients with advanced disease, suffering may result from any or all of the various causes and the effects are additive. The term Total Suffering is used to describe the sum of a patient's suffering, which is what has to be addressed in palliative care (Figure 2).

Table 1 - WHO definition of palliative care

Palliative care is an approach that improves the quality of life of patients and their families facing the problems associated with life-threatening illness through the prevention and relief of suffering by means of early identification and impeccable assessment and treatment of pain and other problems, physical, psychosocial and spiritual.

Palliative care
Provides relief from pain and other distressing symptoms
Affirms life and regards dying as a normal process
Intends neither to hasten or postpone death
Integrates the psychological and spiritual aspects of patient care
Offers a support system to help patients live as actively as possible until death
Offers a support system to help the family cope during the patient's illness and in their own bereavement
Uses a team approach to address the needs of patients and their families including bereavement counselling if indicated
Will enhance quality of life and may also positively influence the course of illness
Is applicable early in the course of illness in conjunction with other therapies that are intended to prolong life such as chemotherapy or radiation therapy and includes those investigations needed to better understand and manage distressing clinical complications

The components of palliative care follow logically from the causes of suffering (Figure 3). Each has to be addressed in the provision of comprehensive palliative care. Treatment of pain and physical symptoms are usually addressed first because it is not possible to deal with the psychosocial aspects of care if a patient has unrelieved pain or other distressing physical symptoms. Cultural factors and religious concerns may be the source of considerable suffering. All patients with a terminal illness experience some spiritual (or existential) suffering although, in the presence of unrelieved pain or physical symptoms, it may go unsaid or unheard.

Pain
Physical symptoms
Psychological problems
Social difficulties
Cultural factors
Spiritual concerns

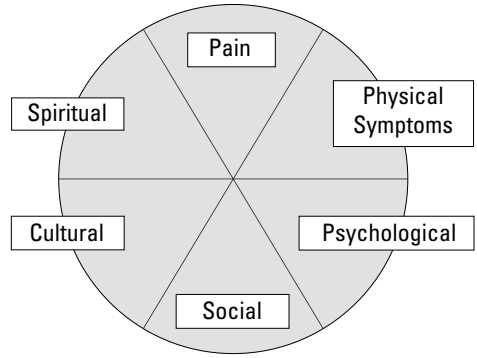


Figure 1 The causes of suffering

Pain
+ physical symptoms
+ psychological problems
+ social difficulties
+ cultural factors
+ spiritual concerns
= Total Suffering

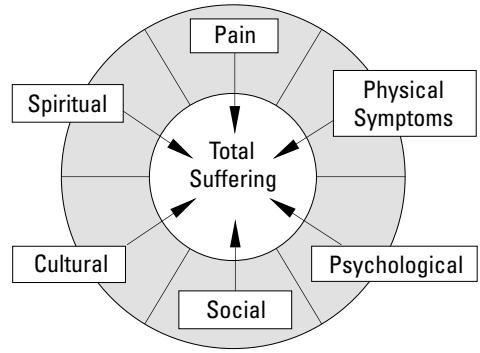


Figure 2 Total suffering

Suffering	**Care**
pain	treatment of pain
+ other physical symptoms	& other physical symptoms
+ psychological problems	& psychological problems
+ social difficulties	& social difficulties
+ cultural factors	& cultural factors
+ spiritual concerns	& spiritual concerns
= Total Suffering	= Multidisciplinary Palliative Care (Total Care)

Figure 3 Aspects of suffering and the components of palliative care

The various aspects of suffering are interdependent. Untreated or unresolved problems relating to one cause of suffering may cause or exacerbate other aspects of suffering. To take pain as an example, unrelieved pain can cause or aggravate problems related to any or all of the other causes of suffering (Figure 4a). The importance of these inter-relationships is that these other components of suffering will not be treated successfully until the pain is relieved. Conversely, pain may be caused or aggravated by problems relating to other causes of suffering (Figure 4b). In this situation, no amount

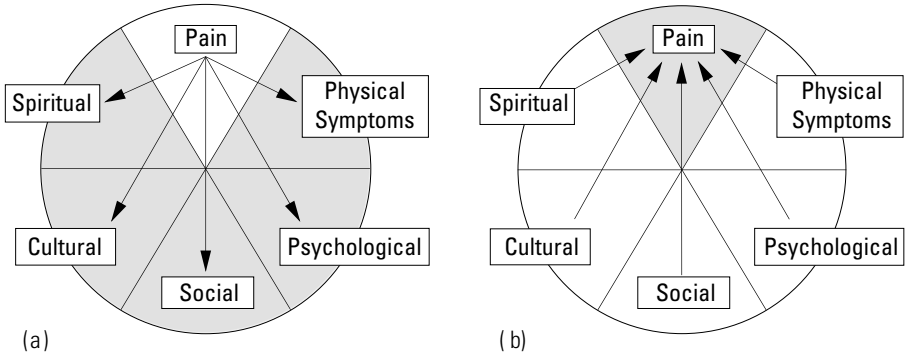


Figure 4 Interdependence of the various causes of suffering. (a) Unrelieved pain may cause or aggravate problems related to any of the other aspects of suffering. (b) Unresolved problems relating to any other aspects of suffering may cause or aggravate pain.

of well-prescribed analgesia will relieve the patient's pain until the other aspects of suffering that are aggravating the problem of pain are addressed. Thus, successful pain control requires attention to some or all of the other aspects of care and suffering and this makes a multidisciplinary approach to assessment and treatment mandatory.

Multidisciplinary Approach to Palliative Care

Established palliative care services work as a multidisciplinary or inter-professional team (Table 2). Multidisciplinary is the term that used to be applied to palliative care teams, but if the individuals work independently and there are no regular team meetings, patient care may become fragmented. The term inter-professional is now used for teams that meet on a regular basis to discuss patient care and develop a unified plan of management for each patient.

Table 2 - The multidisciplinary team
Medical staff
Nursing staff
Social worker
Physiotherapist
Occupational therapist
Dietician
Psychologist (or liaison psychiatrist)
Chaplain (or pastoral care worker)
Volunteers
Other personnel, as required
Family members
Patient

INTEGRATION OF PALLIATIVE CARE INTO CLINICAL CARE

Palliative Care is Active Therapy

Many health care workers believe that palliative care is the "soft option" to be adopted when "active" therapy stops. This is untrue. Palliative care, addressing all the patient's physical and psychosocial problems, is very active therapy. Symptomatic and supportive palliative care should be practiced before the terminal phase of the illness, in some instances at the same time as the patient is still receiving therapy directed at the underlying disease. Even when such "active" therapy is no longer being given, palliative care remains medically active therapy. Active intervention such as medical treatment for hypercalcaemia, radiotherapy for pain or spinal cord compression, and surgery for fractures or visceral obstruction are common.

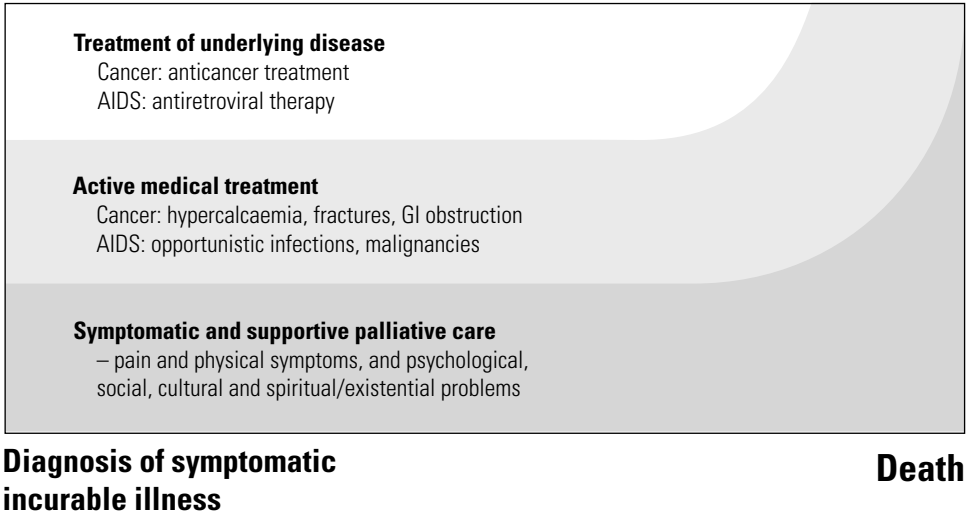
Seamless Integration

Palliative care has in the past been regarded as the care employed when all avenues of treatment of the underlying disease are exhausted and further active medical treatment considered inappropriate (Figure 5).

Figure 5- A traditional view of palliative care. Symptomatic and supportive palliative care is withheld until all avenues of treatment for the underlying disease are exhausted and the treatment of other medical problems considered inappropriate.

Treatment of the underlying disease	Palliative Care
Active treatment of medical problems	
Diagnosis of Symptomatic incurable illness	**Death**

Figure 6 - A modern view of palliative care. Symptomatic and supportive palliative care is complementary to, and seamlessly integrated with, active treatment of the underlying disease.


Treatment of underlying disease
Cancer: anticancer treatment
AIDS: antiretroviral therapy
Active medical treatment
Cancer: hypercalcaemia, fractures, GI obstruction
AIDS: opportunistic infections, malignancies
Symptomatic and supportive palliative care
– pain and physical symptoms, and psychological, social, cultural and spiritual/existential problems
Diagnosis of symptomatic incurable illness
Death

The principles and practices of multidisciplinary palliative care should be initiated at such time as the patient is symptomatic of active, progressive, incurable disease, and should never be withheld until such time as all modalities of therapy for the underlying disease have been exhausted. Palliative care is complementary to active treatment for the underlying disease. It should be implemented long before the terminal phases of the disease and integrated in a seamless manner with other aspects of care (Figure 6). It employs a holistic approach encompassing all aspects of a patient's suffering, which is a prerequisite for successful palliative care but is often lacking in disease-orientated medicine.

PRINCIPLES OF PALLIATIVE CARE

The principles of palliative care (Table 3, below) might simply be regarded as those of good medical practice.

Table 3 - Principles of palliative care
Attitude to Care
Caring attitude
Commitment
Consideration of individuality
Cultural considerations
Consent
Choice of site of care
Communication
Communication amongst health care professionals
Communication with patients and families
The Care
Clinical context: appropriate treatment
Comprehensive and multidisciplinary
Care excellence
Consistent
Co-ordinated
Continuity
Crisis prevention
Caregiver support
Continued reassessment

A Caring Attitude. A caring attitude involves sensitivity, sympathy and compassion, and demonstrates concern for the individual. There is concern for all aspects of a patient's suffering and not just the medical problems. It also implies a non-judgmental approach in which personality, intellect, ethnic origin, religious belief or any other individual factors do not prejudice the delivery of optimal care.

Consideration of Individuality. The practice of categorizing patients by their underlying disease, based on the similarity of the medical problems encountered, fails to recognize the psychosocial features and problems that make every patient a unique individual. These unique characteristics can greatly influence suffering and need to be taken into account when planning the palliative care for individual patients.

Cultural Considerations. Ethnic, racial, religious and other cultural factors may have a profound affect on a patient's suffering. Cultural differences are to be respected and treatment planned in a culturally sensitive manner.

Consent. The consent of a patient, or those to whom the responsibility is delegated, is necessary before any treatment is given or withdrawn. The majority of patients want shared decision making although physicians tend to underestimate this. Having assessed what treatment is appropriate or inappropriate, this is discussed with the patient. In most instances, adequately informed patients will accept the recommendations made.

Choice of Site of Care. The patient and family need to be included in any discussion about where the patient is to be managed. Patients with a terminal illness should be managed at home whenever possible, and if the socioeconomic conditions are given.

Communication. Good communication between all those involved in a patient's care is essential and is fundamental to many aspects of palliative care. The basic rules for communication with patients are listed in Table 4.

Table 4- Communicating with patients
Basic rules
conduct the interview in person (not by telephone)
ensure privacy, prevent interruptions
sitting down (not standing over the bed)
allow enough time
at least one family member or friend should accompany the patient
Providing information
the medical situation
what treatment can be offered
the possible benefits and burdens of any treatments
avoid precise prognostication
as much or as little information as they want
Information should be conveyed
in a caring and sympathetic way, not abruptly or bluntly
in a way they can understand
clearly (avoiding euphemisms)
truthfully
in a positive manner
use independent interpreters

Clinical Context: Appropriate Treatment. All palliative treatment should be appropriate to the stage of the patient's disease and the prognosis. Over-enthusiastic therapy and patient neglect are equally deplorable. Palliative care has been accused of the medicalization of death, and care

must be taken to balance technical interventions with a humanistic orientation to dying patients. The prescription of appropriate treatment is particularly important in palliative care because of the unnecessary additional suffering that may be caused by inappropriately active therapy or by lack of treatment. When palliative care includes active therapy for the underlying disease, limits should be observed, appropriate to the patient's condition and prognosis. Where only symptomatic and supportive palliative measures are employed, all efforts are directed at the relief of suffering and the quality of life, and not necessarily at the prolongation of life.

Comprehensive Multidisciplinary Care. As discussed above, the provision of total or comprehensive care for all aspects of a patient's suffering requires a multidisciplinary approach.

Care Excellence. Palliative care should deliver the best possible medical, nursing and allied health care that is available and appropriate.

Consistent Medical Care. Consistent medical management requires that an overall plan of care be established for each patient. This will reduce the likelihood of sudden or unexpected alterations, which can be distressing for the patient and family.

Coordinated Care. Coordination of care involves the effective organization of the work and efforts of the members of the palliative care team, to provide maximal support and care to the patient and family. Care planning meetings, to which all members of the team can contribute, and at which the views of the patient and the family are presented, are used to develop a plan of care for each individual patient.

Continuity of Care. The provision of continuous symptomatic and supportive care from the time the patient is first referred until death is basic to the aims of palliative care. Problems most frequently arise when patients are moved from one place of care to another and ensuring continuity of all aspects of care is most important.

Crisis Prevention. Good palliative care involves careful planning to prevent the physical and emotional crises that occur with progressive disease. Many of the clinical problems can be anticipated and some can be prevented by appropriate management. Patients and their families should be forewarned of likely problems, and contingency plans made to minimize physical and emotional distress.

Caregiver Support. The relatives of patients with advanced disease are subject to considerable emotional and physical distress, especially if the patient is being managed at home. Particular attention must be paid to their needs as the success or failure of palliative care may depend on the caregivers' ability to cope.

Continued Reassessment. Continued reassessment is a necessity for all patients with advanced disease for whom increasing and new clinical problems are to be expected. This applies as much to psychosocial issues as it does to pain and other physical symptoms.

BARRIERS TO PALLIATIAVE CARE

Even in developed countries, many patients with advanced disease do not receive palliative care and some are referred too late in the course of their disease to benefit from treatment. The reasons for this may relate to the physician, the patient, or to social factors. Some of the barriers are listed in Table 5.

Table 5 - Barriers to palliative care
Physician
Late referral
poor prognostication
lacks communication skills to address end-of-life issues
Reluctant to refer
doesn't understand or believe in palliative care
loss of control, loss of income
lack of institutional standards for end-of-life care
Patient
Believe prognosis better than what they are told
Unrealistic expectation of disease response
Patient-family disagreement about treatment options
Lack of advance care planning
Social factors
Ethnic minorities, language barriers
Rural communities
Poor or underprivileged
Policy factors
Palliative care is not part of the health care system
No reimbursement for palliative/hospice care service
Restrictive laws and regulations which impede access to opioids

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2 Morbidity and Mortality in Developed and Developing Countries

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INTRODUCTION

The World Health Organization estimates that 56.5 million deaths occurred worldwide in 2001. Approximately seventy six percent of these deaths occurred in the developing regions, where over three-fourths of the people in the world live. Thirty-three million deaths were attributed to non-communicable conditions, followed by 18.3 million due to communicable conditions, and 5.1 million from unintentional and intentional injuries. Based on these estimates, non-communicable conditions, including cancers and cardiovascular diseases, accounted for 58.5% of the total mortality in the world in 2001. Communicable diseases, maternal and perinatal conditions and nutritional deficiencies, accounted for 32.5% of all deaths, followed by intentional and unintentional injuries, that comprise nine percent of the total world mortality (1). Table 1 shows the percentages from each broad cause of death for the world and the six major world regions as categorized in the World Health Report, 2002.

SPECIFIC LEADING CAUSES OF DEATH IN 2001

Cardiovascular diseases, such as ischemic heart disease and cerebrovascular disease, currently the world's leading causes of death, accounted for approximately twenty nine percent of all deaths (16,585,000) in 2001. More than ten million of the 16.5 million who died of cardiovascular diseases were from the developing world. These top causes were followed by a series of communicable diseases such as acute respiratory infections, HIV/AIDS, diarrhoeal diseases and tuberculosis. Other important causes of death were due to noncommunicable conditions such as lung/tracheal cancer and chronic obstructive pulmonary disease that are associated with tobacco usage, combustion of fossil fuels and indoor burning of solid fuels (1). Cumulatively, the ten leading causes of death accounted for over half of all deaths (See Table 2).

Death patterns, however, vary greatly across the world. WHO classifies the 191 Member States into six world regions that represent distinct geographic areas with different levels of economic and demographic development: Africa; the Americas; Eastern Mediterranean; Europe; South-East Asia; and Western Pacific. Mortality data from these regions show substantial differences in patterns of mortality. Cardiovascular diseases are the top cause of death in five of the six world regions. Yet in Africa, where seventy percent of the people with HIV infection in the world live, HIV/AIDS ranks as the leading cause of mortality, and accounts for an alarming nineteen percent of the total deaths

in this region. Worldwide, HIV/AIDS is the fourth cause of death, although it ranked 42nd in the European and Eastern Pacific regions. Diarrhoeal diseases ranked 22nd in the European region, but in contrast, is among the top five leading causes of mortality in the African, Eastern Mediterranean and South-East Asian regions, and the sixth leading cause of death worldwide (1).

Table 1. Percentages of deaths in the world and WHO Regions by broad cause categories, 2001.

Regions	Broad Causes of Death		
	Communicable diseases	Noncommunicable conditions	Injuries
World	*33*	58	9
Africa	70	23	7
Americas	21	68	11
Eastern Mediterranean	30	57	13
Europe	7	86	7
South-east Asia	38	51	11
Western Pacific	15	76	9

- *Data extracted from the World Health Report, 2002.*

While WHO's characterization of the world's mortality patterns by geographic region provides a useful summary of the death rates around the world, important differences exist within these major regions. A closer examination of mortality data within regions shows distinctive patterns by levels (low and high) of child and adult mortality. WHO therefore further divides the Member States into five mortality strata based on their levels of child and adult mortality. The six WHO world regions divided into mortality strata results in fourteen epidemiological sub regions (see Table 3). This sub-classification of the world regions reveals substantial differences in death rates and patterns across sub regions. For example, in the Americas, the leading cause of death is cardiovascular diseases (28%). Yet, in the poorer countries like Bolivia, Haiti and Nicaragua, that experience both high child and high adult mortality, the number of deaths attributed to infectious and parasitic diseases is greater than those attributed to cardiovascular diseases (1). Table 4 illustrates the variations in the mortality patterns between developed nations, developing nations with low mortality rates and developing nations with high mortality rates.

Table 2. Leading Causes of Mortality throughout the World by WHO Regions

	All countries		Africa		The Americas		Eastern Mediterranean		Europe		Southeast Asia		Western Pacific	
Deaths	rank	% of total	rank	% of total	rank	% of total	rank	% of total	rank	% of total	rank	% of total	rank	% of total
Ischematic heart disease	1	12.7	9	3.1	1	16.4	1	12.6	1	25.1	1	13.6	3	8.3
Cerebrovascular disease	2	9.6	10	2.9	2	7.7	5	5.2	2	15.2	3	7.4	1	16.6
Acute lower respiratory infections	3	6.8	2	9.6	5	3.8	2	9.2	4	3.1	2	9.4	4	5.0
HIV/AIDS	4	5.1	1	20.6	14	1.5	16	1.4	41	0.3	8	3.1	32	0.5
Chronic obstructive pulmonary disease	5	4.7	16	1.1	6	3.8	8	2.1	5	3.0	7	4.2	2	11.6
Perinatal conditions	6	4.4	5	5.4	7	2.8	4	7.6	23	0.7	4	7.1	8	3.0
Diarrheal diseases	7	3.5	4	6.6	17	1.3	3	7.9	45	0.3	5	5.5	25	0.6
Tuberculosis	8	2.9	8	3.2	28	0.8	6	3.2	20	0.8	6	4.9	9	3.0
Cancer of trachea/ bronchus/lung	9	2.2	46	0.2	4	3.8	23	0.7	3	3.8	16	1.1	6	3.4
Road traffic accidents	10	2.1	11	1.7	9	2.4	7	2.5	12	1.3	9	2.4	11	2.5

- Data extracted from the World Health Report, 2002

Table 3. Percentages of deaths in the world by broad cause and mortality stratum in WHO Regions, estimates for 2001.

Regions	Broad Causes of Death		
	Communicable diseases, maternal & perinatal conditions & nutritional deficiencies	Noncommunicable conditions	Injuries
World	33	58	9
Africa – high child, high adult mortality	68	25	7
Africa – high child, very high adult	73	20	7
America – very low child and adult	6	88	6
America – low child and adult	19	69	12
America – high child and adult	36	53	11
Eastern Mediterranean- low child and adult	18	67	15
Eastern Mediterranean- high child and adult	49	42	9
Europe- very low child and adult	6	89	5
Europe- low child and adult	10	84	6
Europe- low child and high adult	4	83	13
South-East Asia- low child and adult	29	58	13
South-East Asia- high child and adult	42	48	10
Western Pacific – very low child & adult	12	81	7
Western Pacific – low child & adult	15	75	10

Table 4. Percentages of deaths in the world by broad cause categories, level of development, and mortality strata, 2001.			
Levels of Development	**Communicable diseases, maternal & perinatal conditions & nutritional deficiencies**	**Noncommunicable conditions**	**Injuries**
World	*33*	*58*	*9*
Developed	*8*	85	*7*
Low mortality developing	*20*	*67*	*13*
High mortality developing	*54*	*38*	*8*

- *Data extracted from the World Health Report, 2002.*

Historically, developing nations have experienced high mortality from communicable diseases, maternal and perinatal conditions and nutritional deficiencies. Although death rates attributed to these conditions were somewhat reduced at one point during the 20th century in many nations due largely to improvement in basic sanitation, many developing countries are again facing a return of greater death rates caused by an increasing number of infectious and parasitic diseases. In the past 10 years, emerging infectious diseases such as malaria, dengue, tuberculosis, and cholera have caused over one fourth of the cumulative deaths in developing nations. In addition, the AIDS epidemic alone is driving a significant and negative shift in demographic indicators. In Sub-Saharan African, it is estimated that ten percent of the adult population is infected with the HIV virus, and AIDS deaths are responsible for a significant double-digit drop in life expectancy over the past two decades (2-5).

THE EPIDEMIOLOGICAL TRANSITION AND THE DOUBLE BURDEN OF DISEASES IN DEVELOPING NATIONS

Despite many of the strides made against communicable, maternal, perinatal and nutritional conditions in many parts of the world throughout the twentieth century, these diseases remain a significant source of illness and premature death in many developing nations. Almost 18.4 million deaths in 2001 resulted from these causes, and roughly eighty percent occurred in high mortality, developing regions, primarily in nations from the African Region and the poorer South-East Asian nations such as India and Bangladesh. WHO estimates, for example, that there are 1.7 million deaths worldwide each year due to infectious diarrhea. Ninety percent of these deaths occur in children and practically all take place in developing nations (1). However, many developing nations and regions are experiencing a transition in terms of their death patterns. Deaths due to noncommunicable conditions such as cancer, emphysema and cardiovascular disease are rising sharply, due primarily to shifts in the population structure to older ages and lifestyle factors, most notably, increases in tobacco consumption. In fact it is estimated that by the year 2020, diseases associated with tobacco

consumption will result in more deaths than any one disease, including HIV. Consequently, developing countries are expected to face a significant increase in mortality due to non-communicable conditions (6).

Projections from the joint WHO and Harvard School of Public Health landmark 1996 publication entitled, *The Globlal Burden of Disease and Injury Series,* suggest that deaths from noncommunicable diseases will reach 49.7 million by the year 2020, representing a seventy seven percent increase in absolute numbers from 1990. This means that many of the poorer nations of the world are being faced or will soon be faced with a double burden of diseases, a combination of the traditional leading causes of death and illness with the new emerging noncommunicable ones (6).

Table 4 shows the percentage from each broad cause of death for developed and developing regions of the world as categorized in the World Health Report, 2002. Interestingly, many developing regions are already experiencing a higher percentage of deaths from noncommunicable conditions than from the traditional infectious diseases. Most of these developing nations are those with relatively low mortality rates. For instance, following cardiovascular diseases, cancer is now the second leading cause of death among adults in most of the nations of Latin America and the Caribbean (7). In China, a low mortality nation from the Western Pacific Region, there are over 4.5 as many deaths from noncommunicable conditions as from communicable diseases (6). Numerous developing nations from the Eastern Mediterranean (e.g. Jordan), and South East Asia (e.g., Tailand) are also experiencing a greater proportion of deaths attributable to noncommunicable conditions.

VARIATIONS IN MORTALITY RATES AND LIFE EXPECTANCY BY REGION AND NATIONS

Adult and child mortality rates and life expectancy estimates in the six major world regions for both females and males are illustrated in Tables 5-7. The African region has the highest adult and child mortality rates in the world. The highest adult mortality occurs in Zimbabwe, where it was estimated at 812 per 1000 inhabitants in 2001. Extremely high adult mortality rates, ranging from 708 – 782/1000 also occur in nations such as Botswana, Zambia, Swaziland, and Lesotho. Nations such as Sierra Leone and Angola have alarmingly high child mortality rates of approximately 300 per 1000 children. People from the African region also die much younger than those from all of the other regions of the world. Specifically, the lowest life expectancy rates are found in the poorer African nations such as Sierra Leone, Angola, Malawi, Zambia and Zimbabwe, where life expectancy ranges between 34 and 37 years of age. Very low life expectancy rates are also evident in Haiti and Angola (8).

The European region has the lowest adult and child mortality in the world. The nation with the lowest adult mortality is San Marino, (estimated at 62 per 1000 inhabitants) followed by nations such as Sweden, Iceland, Japan, and Singapore, with mortality rates ranging from 69 to 73 per 1000 inhabitants. Iceland and Sweden have the lowest child mortality rates in the world (3.5 per 1000), and every Western European nation has child mortality rates of less than ten. Other nations such as Japan, Israel, Chile and Cuba also have rates below ten. People in Japan live longer than those from all other nations, where life expectancy is estimated at 81 years of age. Very high life expectancy rates ranging from 79 to 80 years of age are also found in wealthier nations such as Switzerland, Sweden, Iceland, Canada and Italy (8).

Table 5. Adult mortality by regions (per 1000), 2001.			
REGION	**Total**	**Males**	**Females**
Africa	462	496	428
South-East Asia	246	280	212
Eastern Mediterranean	210	237	183
Western Pacific	193	224	162
Americas	180	221	139
Europe	144	196	93

WHO Key indicators, 2001.(8)

Table 6. Child mortality by regions (per 1000), 2001.			
REGION	**Total**	**Males**	**Females**
Africa	151	158	145
South-East Asia	69	69	68
Eastern Mediterranean	67	69	65
Western Pacific	42	45	38
Americas	30	32	27
Europe	18	20	16

Table 7. Life expectancy at birth by regions (years), 2001.			
REGION	**Total**	**Males**	**Females**
Africa	50	48	51
South-East Asia	64	62	65
Eastern Mediterranean	66	64	68
Western Pacific	69	66	71
Americas	71	68	74
Europe	74	70	77

WHO Key indicators, 2001.(8)

GENDER DIFFERENCES

Male mortality rates are consistently higher than female rates for all of the six world regions. This finding is consistent across nations with the exceptions of Saudi Arabia, Qatar, and Bangladesh,

where higher rates have been estimated for women. The largest mortality difference between men and women occurs in the Russian Federation, followed closely by other nations formerly of the USSR, such as the Ukraine, Belarus, Estonia and Latvia and also Haiti of the Americas. Indeed, males between the ages of 15 and 60 from the former USSR and European socialist bloc have a 28% risk of dying, a phenomenon largely attributable to higher rates of noncommunicable diseases and an elevated risk of death from injury.(6) Although male child mortality rates are consistently higher than female rates for all of the six world regions, several countries such as India, Bangladesh, Maldives, Nepal and China experience a higher female child than male child mortality. Women, on average, live roughly two to four years longer than men. However, men in some of the nations of the former Soviet Union live significantly less than their female counterparts. Men in Russia for example, live on average 13.4 years less than women. Men from Belarus, Ukraine, Estonia, Latvia, Lithuania, Seychelles and Haiti also live approximately nine to eleven years less than their female counterparts (8).

INTERNATIONAL BURDEN OF DISEASE AND PALLIATIVE CARE – FUTURE DIRECTIONS

International mortality indicators should be considered in the context of changing patterns of disease. Trends over the past few decades show that, although communicable diseases continue to account for a significant proportion of total mortality in regions like Africa, Southeast Asia and Latin America, non-communicable conditions, including heart disease, lung cancer, and injuries, are expected to increase dramatically in all countries, including developing nations, over the next two decades. These projections, however, are highly tentative, as rapid, man-made, global changes whose consequences are yet to be determined, continue to disrupt ecological systems. Climate changes as a result of global warming, urbanization, economic integration and globalization and growing antibiotic resistance, will continue to influence the impact of infectious and parasitic diseases around the world (9).

Data from the World Health Organization and other international health agencies and organizations indicate that substantial differential patterns of morbidity and mortality exist between developed and developing countries. However, estimating mortality varies widely among nations, and many developing countries have only limited capabilities to produce reliable mortality data and health statistics. Comparability of mortality data across nations may therefore present significant methodological problems including but not limited to different reporting and enumeration systems, changing and varied practices in the coding of causes of death, timeliness of reported data, variation in assessing the correct underlying cause of death, and ill-defined mortality categories. However, the existing data and that which was presented above, although imperfect, provide us with a benchmark from which to work from and target our attention, especially in relation to palliative care.

As noted above, the epidemiological transition which is occurring in developing countries, (primarily those with lower mortality) means that the major causes of death are shifting rapidly from communicable, maternal and perinatal causes to noncommunicable, chronic causes of death such as cancer, or those once mainly associated with the developed world (10). Countries that have yet to conquer the traditional communicable causes of death and illness which are linked highly to poverty and underdevelopment are concurrently facing rapid increases in those illnesses once associated with modernization, and now with globalization (10). This “double burden” of disease and mortality has most certainly required a call to action that includes the provision of adequate palliative care among many other things.

Table 8. WHO Regions and member states by mortality strata, 2001.					
WHO Regions	**Mortality Strata**				
	Very low child, very low adult	**Low child, low adult**	**Low child, high adult**	**High child, high adult**	**High child, very high adult**
African Region				AFR-D (Algeria, Angola, Nigeria)	AFR-E (Congo, Mozambique, South Africa)
Region of the Americas	AMR-A (USA, Canada, Cuba)	AMR-B (Argentina, Brazil, Mexico)		AMR-D (Bolivia, Haiti, Nicaragua)	
Eastern Mediterranean Region		EMR-B (Cyprus, Jordan, Tunisia)		EMR-D (Afghanistan, Iraq, Yemen)	
European Region	EUR-A (Germany, Greece and Israel)	EUR-B (Azerbaijan, Bulgaria, Poland)	EUR-C (Estonia, Hungary, Russian Federation)		
South-East Asia Region		SEAR-B (Indonesia, Sri Lanka, Thailand)		SEAR-D (Bangladesh, Democratic People's Republic of Korea, India, Nepal)	
Western Pacific Region	WPR-A (Australia, Japan, Singapore)	WPR-B (China, Republic of Korea, Viet Nam)			

- *Data extracted from the World Health Report, 2002.*

Globally, palliative care is an area that is often overlooked, especially in developing nations, where most of the people in need of palliative care are. The cases of AIDS and cancer in the world illustrate well these points. AIDS projections for 53 of the most affected countries indicate that although the probability of being infected with HIV will decrease at the end of the current decade, excess mortality due to HIV will increase by a factor of 5 by 2050 or from 53 million excess deaths in the current decade to 278 million by the 2000 mid-century.[10] Similarly, malignant neoplasms are among the major noncommunicable causes of death worldwide and accounted for 12.6% of the total global deaths in 2001.1 The incidence of cancer and cancer death rates have increased substantially in recent years and cancer is now emerging as a major public health problem in developing countries. *The World Cancer Report*, issued recently by the International Agency for Research on Cancer (IARC), projects that global cancer rates may increase by fifty percent from 10 million new cases worldwide in 2000, to 15 million new cases in 2020, an increase primarily due to the ageing of populations and adoptions of unhealthy behaviors such as smoking. The report, however, suggests that one third of cancers

could be prevented, another third could be cured and the remaining third could be provided with quality, inexpensive palliative care(11). If these projections are met, millions with HIV and nearly five million people with cancer in the world will require palliative care and pain relief services by the year 2020 (11).

The need for the provision of palliative care is especially pronounced in developing nations where the incidence of cancer is on the rise and adequate palliative care is rarely available. Fifty percent of the world's new cancer cases and deaths are already occurring in developing nations and roughly eighty percent of these cancer patients are already incurable at the time diagnosis. Despite these rising rates, adequate palliative care is unavailable to 80-90 percent of cancer patients in these countries. These findings demonstrate a need for both better detection programs and provision of palliative care (11).

The new *World Cancer Report* calls on all countries to establish comprehensive national cancer control programs aimed at: reducing the incidence of cancer through primary prevention; providing earlier diagnosis and curative treatments; and improving the quality of life for cancer patients and their families through the delivery of adequate palliative care and pain relief (11). In light of the rapid and dramatic transition to noncommunicable causes of mortality in many of the developing regions in conjunction with the perseverance of the traditional killers, the call for action has been made. It is now up to governments to formulate palliative care policies that emphasize changes within their healthcare systems that integrally and comprehensively include palliative care as a principal component of their national healthcare policies. The provision of quality palliative care could be a realistic and humane alternative to the neglect experienced by millions of the world's dying.

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3 Socioeconomic, Cultural and Political Issues in Palliative Care

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INTRODUCTION

Improvements in technology have accelerated the transfer of information and knowledge from developed to developing countries. But globalization has benefited only a small percentage of the population, especially in developing countries (1). Approximately one fifth of the world's population live on less than US$1 per day and almost a half live on less than US $2 per day. At the Millennium Summit of the United Nations (UN) in September 2000 country leaders called for "a dramatic reduction in poverty and marked improvements in the health of the poor" by adopting the Millennium Development Goals (MDG) in the Report on Macro Economics and Health (MEH) (2). discussed further in this chapter. The core findings of this report are that disease burden in the poorest countries constitutes a fundamental barrier to economic advancement and that millions of poor people die from infectious diseases that are preventable, and treatable, because they lack access to the needed health services.

DEMOGRAPHICS

The total world population is 6.3 billion of which 4.1 billion, or 65%, live in developing countries (3). Ninety six percent of the births, 77% of the deaths and 99% of the global natural increase (the difference between the number of live births and deaths) occur in the developing world. On the other hand, if present trends continue, the natural increase in developed nations will be negative in the near future and any increase or decrease in the population will be determined by migration. Globally, the number of older persons (60 years or more) will nearly triple, increasing from 606 million in 2000 to nearly 2 billion by 2050. Whereas 6 of every 10 of those older people live today in less developed countries, by 2050 8 of every 10 will do so (4).

In the last decade, there has been a major shift from rural to urban centers resulting in very large cities and isolated rural areas. Three billion people (almost every other person) live in an urban area, and by 2030 over 60 percent of the world's population (4.9 billion out of 8.1 billion people) will reside there. Table 1, page 26, shows the cities with 10 million inhabitants or more during various years. By 2010, Lagos is projected to become the third largest city in the world, after Tokyo and Mumbai (Bombay). Milan, Essen and London will disappear from the 30 largest cities list, and New York, Osaka and Paris will slip farther down (3).

Table 1 – Population of cities with 10 million inhabitants or more, 1950, 1975, 2001 and 2010 (millions)							
1950		**1975**		**2001**		**2010**	
City	**Pop**	**City**	**Pop**	**City**	**Pop**	**City**	**Pop**
1. New York	12.3	1. Tokyo	26.5	1. Tokyo	26.5	1. Tokyo	28.7
		2. New York	15.9	2. Sao Paulo	18.3	2. Bombay	27.4
		3. Shanghai	11.4	3. Mexico City	18.3	3. Lagos	24.4
		4. Mexico City	10.7	4. New York	16.8	4. Shanghai	23.4
		5. Sao Paulo	10.3	5. Bombay	16.5	5. Jakarta	21.2
				6. Los Angeles	13.3	6. Sao Paulo	20.8
				7. Calcutta	13.3	7. Karachi	20.6
				8. Dhaka	13.2	8. Beijing	19.4
				9. Delhi	13.0	9. Dhaka	19.0
				10. Shanghai	12.8	10. Mexico City	18.9
				11. Buenos Aires	12.1	11. New York	17.0
				12. Jakarta	11.4	12. Calcutta	16.5
				13. Osaka	11.0	13. Los Angeles	15.6
				14. Beijing	10.8	14. Delhi	15.2
				15. Rio de Janeiro	10.8	15. Buenos Aires	12.6
				16. Karachi	10.4	16. Metro Manila	11.7
				17. Metro Manila	10.1	17. Rio de Janeiro	11.5
						18. Cairo	11.5
						19. Istanbul	11.4
						20. Osaka	11.0
						21. Tianjin	10.3

The current worldwide rate of urbanization (annual percentage increase of the urban share of the total population) is about 0.8 percent, varying between 1.6 percent for all African countries to about 0.3 percent for all highly industrialized countries. Urbanization of poverty is also increasing: it is estimated that between one-quarter and one-third of all urban households in the world live in absolute poverty. And despite general economic growth, the number of poor in Latin America rose from 44 million to 220 million from 1970 to 2000. More than 40% of the population in Mexico City and 35% in Sao Paulo live at or below the poverty line (5). This phenomenon has a huge impact on the ability of nations to offer appropriate care and affects the capacity of the individuals to access health care services.

In developed countries, families tend to be nuclear (parents and children), they are more mobile and rely on a health care system for the care of the sick and dying. In many developing countries the family structure is the extended family (grandparents, children, grandchildren, uncles and aunts), who tend to live together or nearby, and the burden of care is the responsibility of the entire family. However, with the latest migration trends to urban areas, space has become more limited, living conditions more expensive and in many cases both parents and children are forced to work. This has resulted in the atomization of the traditional structure where families are becoming increasingly fragmented and isolated. Cities have not been able to keep up with the increased demand for care of the elderly and the poor, and the terminally ill. In large urban areas of developing countries, the demand for palliative care results in the over utilization of emergency services in large hospitals.

More than one billion of the world's urban residents live in inadequate housing, mostly in the sprawling slums, and settlements, of developing countries. Over 50% of the population in Mumbai and New Delhi lives in slums, while in Lagos and Nairobi over 60% of the households do not have running water (6). These conditions as well as war and safety concerns, affect accessibility, and negatively impact the development of large scaled public home care programs. However, some developing countries, with the leadership of individuals, have been able to create successful home care palliative care programs like one described in chapter 18 of this publication.

COMMISSION ON MACROECONOMICS AND HEALTH (MEH)

In June 2002, the World Health Organization (WHO) convened a consultation group of senior officials from Ministries of Health, planning and finance, to review possible national responses to the Report of MEH. The Commissioners concluded that investing in people's health is essential for the human and economic development of poor nations and would show that investing in health care for the poor would help millions of people to emerge from poverty, as well as contribute in important ways to overall economic growth.

POVERTY, AFFLUENCE AND THE GLOBAL BURDEN OF DISEASE

Controlling the burden of disease and suffering is a fundamental goal of economic development as the link of health to poverty reduction and long-term economic growth has been demonstrated. Low-income countries with 3.5 billion people, especially the countries in sub Saharan Africa, with almost 650 million people, have far lower life expectancies and mortality rates than the rest of the world as shown in Table 2. Countries with the highest rates of life expectancy are all developed, while the ones with the lowest years of life expectancy at birth are all very poor countries in Sub Saharan Africa as shown in Table 3 (7).

Malaria accounts for roughly 3 per cent of the world's disease burden, but attracts only one sixth of 1% of global Research and Development (R&D) resources in biomedical research, largely because most malaria victims are impoverished and therefore ignored by private industry (8). R&D investments directed at diseases of the poor are likely to have enormous social returns, not only because of direct breakthroughs in science, but also because so little is currently invested in these areas.

In developed countries, the probability of being diagnosed with cancer is more than twice as high as in developing countries. However, in rich countries, some 50 per cent of cancer patients die of

the disease, while in developing countries, 80 per cent of cancer victims already have late-stage incurable tumors when they are diagnosed, pointing to the need for much better detection programs and palliative care. More than 50 per cent of the world's cancer burden, in terms of both numbers of cases and deaths, already occurs in developing countries where only 5% of the resources for cancer treatment reside (9).

Table 2 – Demographic Indicators (1995-2000)

Development Category	Population 1999 (millions)	Annual Average Income (US $)	Life Expectancy at Birth	Infant Mortality (per 1,000 live births)
Least Developed Countries	643	296	51	100
Other low Income Countries	1,777	538	59	80
Lower-Middle Income Countries	2,094	1200	70	35
Upper-Middle Income	573	4900	71	26
High Income	891	25730	78	6
Sub Saharan Africa	642	500	51	92

Table 3 – Life Expectancy at Birth: Countries with the highest and lowest rates (2000-2005)

Country	Life Expectancy	Country	Life Expectancy
Highest		**Lowest**	
Japan	81.6	Zambia	32.4
Sweden	80.1	Zimbabwe	33.1
China, Hong King	79.9	Sierra Leone	34.2
Iceland	79.8	Swaziland	34.4
Canada	79.3	Lesotho	35.1
Spain	79.3	Malawi	37.5
Australia	79.2	Mozambique	38.1
Israel	79.2	Rwanda	39.3
Martinique	79.1	Central African Republic	39.5
Switzerland	79.1	Botswana	39.7
		WORLD	65.4

HEALTH CARE RESOURCES – DIFFERENCES BETWEEN DEVELOPED AND DEVELOPING COUNTRIES

High, and rising, health costs exclude a significant proportion of the poor from essential services, and throw large numbers of families into poverty each year. In most developing countries poor people pay 85%, on average, of the total health services they receive - mostly for unnecessary or inappropriate drugs and treatments. But, also public and private spending is many times wasted, or misdirected. Too much funding is invested in high tech curative efforts for incurable patients in the capital cities, and not enough for the essential medications and interventions to control disease in rural areas. Health care tends to be hospital based whilst community health and support programs are rarely a priority. Training and education of healthcare professionals are poorly defined whilst community education programs which may reduce the burden of healthcare are not given due priority.

There are three problems with the current health financing arrangements of low-income countries: First, there are insufficient levels of health spending per capita. In the least developed countries it averages approximately $13 per person per year of which the public budget contributes only $7. The other low-income countries average approximately $24 per person per year, of which $13 comes from the public sector. Second, the proportion of total health care spending is much lower than in the high-income countries (55 vs. 71%) as seen in Table 4 below. Since public sector spending on health is needed to provide critical public goods and to ensure adequate resources for the poor to gain access to health services, the small size of public spending exacerbates the problem of the overall insufficiency of resources. Third, private spending tends to be out of pocket rather than pre-paid, so there are very little insurance elements and risk pooling built into private spending. Such private spending tends to be inefficient and wasted on high priced medications, unnecessary and futile treatments and poorly trained practitioners with little or nothing spent in palliative care (10).

Table 4 – Domestic Spending on Health - 1997

	Total Spending on Health per capita (US $)	Public Spending on Health per capita (US $)	Percentage
Least Developed Countries	11	6	54.5
Lower Middle Income Developing Countries	93	51	54.8
Upper Middle Income Developing Countries	241	125	51.9
High Income Countries	1,907	1,356	71.1

ACCESS TO AND AVAILABILITY OF PALLIATIVE CARE

Access to palliative care is difficult to measure since palliative care can be defined and perceived differently by individuals in developing and developed countries. For some, palliative care is the delivery of sophisticated medical and nursing care, while for others it may be the provision of a clean bed, food and water, and some nursing care. In many countries palliative care is given informally, outside of the health

care system and provided by caretakers who may or may not have any training and who may or may not receive any compensation or reimbursement for the services provided. Given these differences, and for clarity purposes, whenever addressed in this chapter, palliative care refers to the care approach defined by WHO and endorsed by the International Association for Hospice and Palliative Care (IAHPC) (11).

> *Palliative Care is an approach that improves the quality of life of patients and their families facing the problem associated with life-threatening illness, through the prevention and relief of suffering by means of early identification and impeccable assessment and treatment of pain and other, physical, psychosocial and spiritual problems.*

Palliative Care:

- *Provides relief from pain and other distressing symptoms;*
- *Affirms life and regards dying as a normal process;*
- *Neither hasten nor postpone death;*
- *Integrates the psychological and spiritual aspects of patient care;*
- *Offers a support system to help patients live as actively as possible until death;*
- *Offers a support system to help the family cope during the patient's illness and in their own bereavement;*
- *Uses a team approach to address the needs of patients and their families, including bereavement counseling, if indicated;*
- *Will enhance quality of life, and may also positively influence the course of illness;*
- *Is applicable early in the course of illness, in conjunction with other therapies that are intended to prolong life, such as chemotherapy or radiation therapy, and includes those investigations needed to better understand and manage distressing clinical complications.*

The key constraints and barriers to palliative care can be categorized in five different levels: Community and Household level, Health Services Delivery; Health Sector Policy, Public Policies and Environmental Characteristics. These are summarized and described in Table 5.

PALLIATIVE CARE PUBLIC HEALTH POLICY

The goal to cure at all cost, by using heroic measures, life sustaining support and intensive care units, has to be reevaluated. Technology driven care not only increases the cost of health care delivery but contributes to the deterioration of the relation between the provider and the patient, isolates the patients from his or her relatives and contributes to the burn out syndrome of the health care team. In promoting palliative care, health care planners and providers need to be aware of other outcomes that would benefit from adopting palliative care as a central aspect of dealing with human suffering as a consequence of life threatening illnesses. Physicians especially need to be sensitive to their responsibilities in care and the alleviation of suffering in disease management rather than the wholesome pursuit of goals that may not be achievable.

Palliative Care is not luxurious care for the wealthy as some policy makers and health care workers believe. Care can be provided at very low cost, at home or in very low budget facilities. However, it also needs to be valued accordingly. There are many samples of these facilities in several countries in the world, including Asia, Africa and Latin America.

Table 5 – Levels and Description of Key Constraints and Barriers in Palliative Care	
Levels	**Constraints**
Community and Household Level	Lack of Demand for effective interventions: lack of awareness and insufficient knowledge of palliative care and pain relief strategies. Barriers to use of effective interventions: physical, financial, social barriers: inaccessibility to palliative care programs, poverty, myths on the use of opioids.
Health Services Delivery Level	Shortage and distribution of appropriately qualified staff, insufficient palliative care trained professionals and care takers. Weak technical guidance, program management and supervision Inadequate supplies of drugs and medical supplies due to limits imposed by the laws and regulations and budgetary constraints. Lack of Equipment and infrastructure: No areas for provision of palliative care and limited resources
Health Sector Policy and Strategic Management Level	Weak, overly centralized systems for planning and management: cities monopolize palliative care centers and little is available at the rural level. Weak drug policies and supply systems, restrictive laws and regulations. Inadequate regulation of pharmaceutical and private sector and improper industry practices, including high cost of medications and insufficient distribution to pharmacies. Reliance on donor funding that reduces flexibility and ownership; donor practices that damage country policies.
Public Policies Cutting Across Sectors	Government bureaucracy that maintains an inefficient system running. Poor availability of communications and transport infrastructure – difficulty accessing palliative care services or units
Environmental Characteristics	*A. Governance and overall policy framework* Corruption, weak government, weak rule of law and enforceability of contracts. Political instability and insecurity. Low priority of palliative care in the social sectors. Weak structure for public accountability and patient satisfaction. *B. Physical Environment* Physical environment unfavorable to service delivery: Climatic conditions, or geographical constraints.

It is imperative that a Health Care Policy is developed and created on reasonable goals ensure economic sustainability and cost effectiveness along with compassionate care. The development of policy for palliative care has differed in many countries. In a few countries they have adopted policies at the top level for the provision of palliative care, but with little success in permeating into the public health care system and to the grass roots level, mainly because the structures to place these policies into action do not exist. The outcome is the existence of programs and plans on paper, but little results in the field. It has been demonstrated that if there is little awareness and education, palliative care fails to be incorporated into the system.

In the majority of cases, the development of palliative care has been a "bottom up" approach in which individuals and groups have started programs or initiatives that eventually are incorporated into academic programs and generate enough demand and awareness to motivate health policy changes. The limitation to this system is that it lacks official recognition and therefore reimbursement issues, budget and resource(s) allocation are unavailable, dooming many of these fractured and fragile programs to failure. However, a pragmatic approach for access to palliative care can occur successfully in the absence of policies. The Santo Domingo Report, after the Florianopolis Declaration, is such an example of how programs and individuals at the grass root level were able to draft policy for palliative care that was later adopted by several countries in the Latin American Region (12).

Figure 1 presents the above relationship between health care policy and palliative care. This model is based on the Aday and Andersen Access Framework (13), which was initially developed to guide the first survey of access to medical care conducted in the United States and was later applied to evaluate access to different types of health care (14) It can also be used to analyze access to palliative care. In this model, Health Policy is the starting point for the consideration of predictors of utilization and satisfaction with medical care.

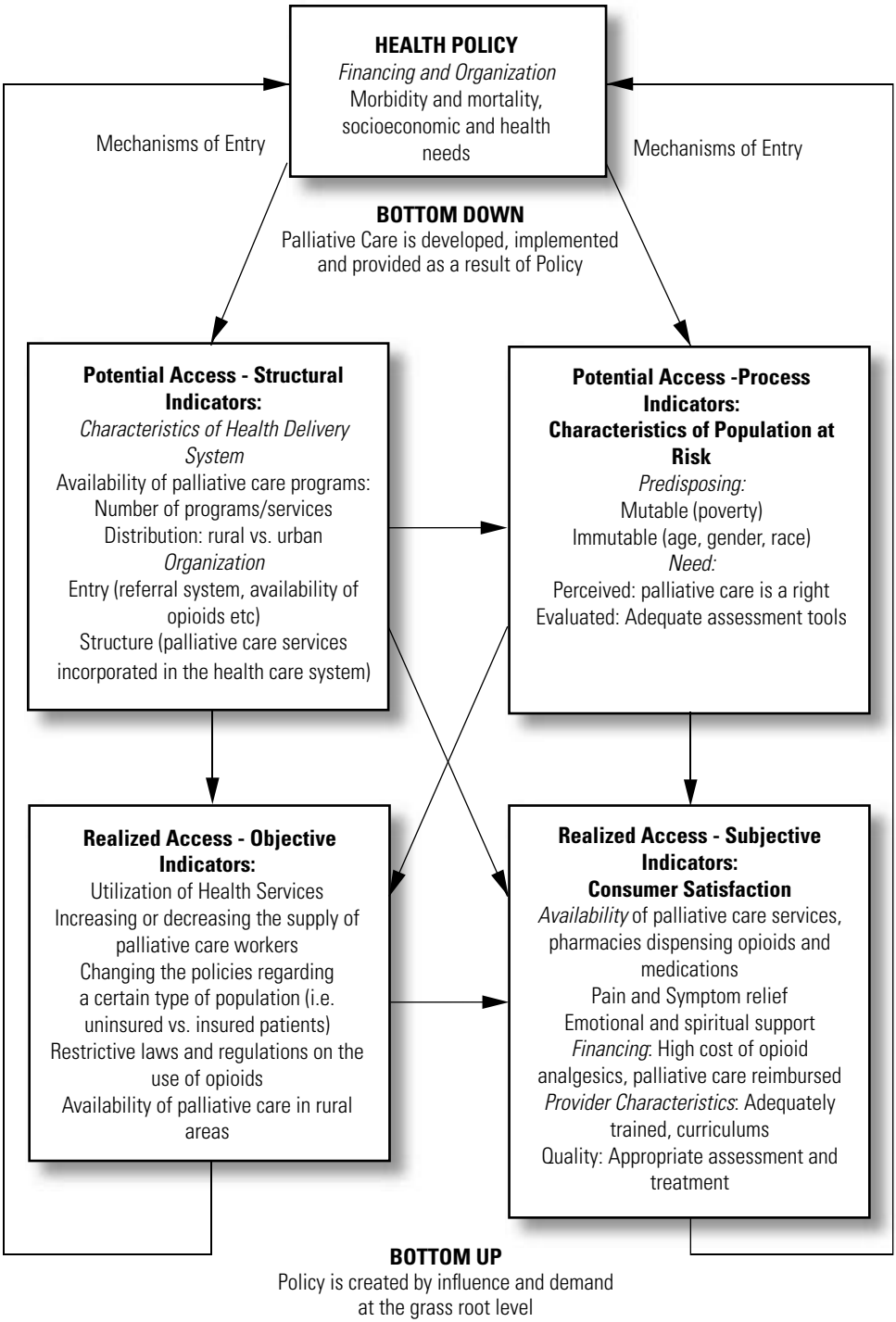
Health policy cannot affect the characteristics of the population at risk, which are the biological and social characteristics such as age, gender, race, and place of residence and are therefore called immutable. Rather, these characteristics are the ones that should determine the basis in which health policy is developed. In turn, health policy affects more enabling variables such as coverage and insurance, which become predictors of potential access and the probability that services will be obtained.

The main categories of access to palliative care as a result of health policy are:
1) Mechanisms of Entry (Access) and Movement: Policy affects the Mechanisms of Entry and Movement throughout the system by limiting the referral systems of patients to palliative care services, the inter-consultation with other medical specialties and the places and times where medications such as opioids can be dispensed.

2) System Structure: Policy affects the Structure by restricting the number of palliative care clinics or facilities, by limiting the number of pharmacies allowed for dispensing opioid analgesics and the number of institutions allowed to provide palliative care to patients in need.

3) Utilization: Health Policy affects utilization directly by increasing, or decreasing, the supply of palliative care workers in an area, or by changing policies that affect a certain type of population (i.e.; coverage for the insured vs. the uninsured) and indirectly, by increasing the number of rural clinics and by making medications available at a low cost and throughout national territories. Some of the laws and regulations also limit the extent to which third party payers can reimburse palliative care services and the medical use of opioids which results in changes in the utilization of services.

Figure 1 – Access to Palliative Care Model (Based on the Aday and Andersen Access to Health Care Model)


HEALTH POLICY
Financing and Organization
Morbidity and mortality, socioeconomic and health needs
Mechanisms of Entry
Mechanisms of Entry
BOTTOM DOWN
Palliative Care is developed, implemented and provided as a result of Policy
Potential Access - Structural Indicators:
Characteristics of Health Delivery System
Availability of palliative care programs:
Number of programs/services
Distribution: rural vs. urban
Organization
Entry (referral system, availability of opioids etc)
Structure (palliative care services incorporated in the health care system)
Potential Access -Process Indicators:
Characteristics of Population at Risk
Predisposing:
Mutable (poverty)
Immutable (age, gender, race)
Need:
Perceived: palliative care is a right
Evaluated: Adequate assessment tools
Realized Access - Objective Indicators:
Utilization of Health Services
Increasing or decreasing the supply of palliative care workers
Changing the policies regarding a certain type of population (i.e. uninsured vs. insured patients)
Restrictive laws and regulations on the use of opioids
Availability of palliative care in rural areas
Realized Access - Subjective Indicators:
Consumer Satisfaction
Availability of palliative care services, pharmacies dispensing opioids and medications
Pain and Symptom relief
Emotional and spiritual support
Financing: High cost of opioid analgesics, palliative care reimbursed
Provider Characteristics: Adequately trained, curriculums
Quality: Appropriate assessment and treatment
BOTTOM UP
Policy is created by influence and demand at the grass root level

Specific indicators of access to palliative care are difficult to apply, as developed countries are now more focused on evidence based approaches, while in many developing countries these criteria are not applicable. However, one of the indicators that can be applied across countries as a measure of access to palliative care is morphine consumption.

MORPHINE USE AS AN INDICATOR OF ACCESS TO PALLIATIVE CARE

For several years, WHO has used morphine consumption as an indicator of adequate access to pain relief, one of the cornerstones of palliative care. Morphine and other potent analgesics are included in the list of Essential Medications.

In 1986, the WHO and its Expert Committee on Cancer Pain Relief and Active Supportive Care developed and effective analgesic method for the relief of cancer pain. The method relies on the permanent availability of opioid analgesics, including morphine, codeine and others. Known as the *Three Step Analgesic Ladder* (15), (described in Chapter 8 of this publication) it has been widely disseminated throughout the world. Still, opioid analgesics are insufficiently available, especially in developing countries, and prescription of morphine is still limited to a small percentage of physicians and in many countries of the world. Some of the reasons why opioids are unavailable in developing countries are: Poverty; Insufficient knowledge on how to asses and treat pain (16); high cost of opioids (17) and; excessively restrictive laws and regulations which impose limits on the dosages and the duration of treatment (18, 19). In several others where morphine is available, misconceptions and lack of education in cancer pain management continue to be a hindrance. The recent trends to globalization have also led to expensive opioids and other drugs to be introduced in some countries where current morphine use is limited. Instead of aiding in the general pain management, such practices may inhibit the further distribution of an effective pain management protocol and inhibit morphine use. The WHO and the International Narcotics Control Board (INCB) have asked governments to ensure availability and accessibility of opioid medications to satisfy the needs of the population (20).

TRENDS IN CONSUMPTION OF OPIOID ANALGESICS

The INCB collects the consumption data yearly from government reports, as required by the United Nations Single Convention on Narcotic Drugs (21). While supply of narcotic drugs for medical purposes remains inadequate, the consumption trends recorded by INCB indicate improvement. The global consumption of morphine has been doubling every five years since 1984. In 2001 it reached a level of 30 tons (22). The trend is, however, mainly due to increasing consumption in a few countries. For 2001, the latest year for which consumption data is available, 77% of the total 30 tons of morphine were consumed in six countries: Australia, Canada, China, France, United Kingdom and USA; the remaining 23% was consumed in the other 133 countries for which data are available. There are 51 developing countries for which there is not registered morphine consumption at all.

INCB also uses a population and dosage adjusted tool called Defined Daily Dosages (DDD) to compare consumption among countries. When adjusted by dosage and population, the countries with the highest consumption are all in developed regions of the world, while those with the lowest consumption are all developing nations, as shown in Table 6 (23).

Table 6 – Average Daily Consumption of Defined Daily Doses per Million Inhabitants (1997-2001)

Country	DDDs
Highest Consumption	
Denmark	6,568
Canada	4,522
Australia	4,365
Austria	3,806
New Zealand	3,728
Iceland	3,686
Sweden	2,946
Portugal	2,902
France	2,896
USA	2,839
Norway	2,765
Switzerland	2,089
Lowest Consumption	
Maldives	1
Burundi	1
Uzbekistan	1
Libyan Arab Jamhiriya	1
Kenya	1
Ghana	1
Syrian Arab Republic	1
Myanmar	2
Malawi	2
Bangladesh	2
Uganda	2
Iraq	2
Swaziland	3
Zambia	3
Bolivia	3
Algeria	3

It is important to note that DDD is a useful tool for comparative studies, but it may not be useful to define the extent to which patients are receiving adequate pain relief. Patients with severe pain, due to chronic conditions such as cancer or acute ones such as infectious diseases, trauma or surgery, may require doses above the 30 mgs/day used in the DDD. Therefore, it can be assumed that the situation for developing countries is far worse than the one described in our study, where patients are severely under dosed.

In developing countries, where analgesic drugs may be difficult to access, there may be tendency to use other medications that may not be entirely appropriate or helpful in the clinical setting. The availability of morphine and opioids needs to be evaluated in terms of compliance, costs and indications whenever possible. The issues of opioids misappropriation, myths about addiction, tolerance and respiratory depression need to be evaluated constantly.

EDUCATIONAL ISSUES

Although many palliative care programs around the world were initiated because a need was realized, educational and training issues were soon to be realized as important. Many palliative care programs that are initiated in developing countries do so by providing the very basic aspects of human needs. Water, nutrition, shelter and nursing care are coupled with human warmth, love and understanding. Grappling with the other confluent aspects of disease and suffering such as pain and symptom control is often more difficult. The often very restrictive regulations affecting opioid use and distribution inhibits good pain control and patients facing end-of-life scenarios may not be the greatest care priority in many healthcare settings.

In dealing with the ravages of illness and disease, the basic educational fundamentals are formed during our training and formative years. Yet palliative care is scarcely dealt with in medical or nursing schools in developing countries, where the need is certainly overwhelming. In countries where palliative care is established, there are multi modal variants of palliative care, and the advent of even sub-specialties of palliative care have emerged. The interdisciplinary teams have become entrenched and much time is now spent in establishing standards of care and the development of research.

With little or no formal basis for palliative care education, much of the delivery of care in developing countries depends on individual initiatives in firstly educating themselves and subsequently educating others. In recent years, two patterns of educational doctrines have surfaced.

Firstly, some educational assistance from palliative care endowed countries has strived to establish and assist in the training of healthcare staff and volunteers from developing countries. These often take the form of short term teaching stints and aim to assist palliative care programs in establishing their own form of education and training needs. Individuals interested in palliative care strive in search of knowledge in order to provide more effective care or to aid them in developing a more strategic system of care. In recent years, the sharing of knowledge through the internet and disbursement of literature has also been helpful. However, glances at palliative care literature reflect the paucity of material originating from developing countries. Surely the documentation of their experience would be of benefit.

Secondly, healthcare and institutions of higher leaning offer placements to healthcare workers from developing countries places within their own training programs. Though individuals undertaking this form of training may derive benefit, they are often exposed to palliative care scenarios that may have little similarities to those they may face in their own countries. Palliative care in many developed countries and in established palliative care medical literature mainly focuses on cancer but in the developing countries, the burden of care encompasses many other diseases that will be mentioned in other aspects of this book. The cost of undertaking training courses in countries with developed palliative care education is often grossly prohibitive. Even short attachments to many established palliative care institutions may also incur a charge to those striving to broaden their knowledge and develop their skills. Palliative care education has become in some cases an economic educational commodity rather than a humanistic approach to the sharing of knowledge.

In many parts of the developing world, palliative care programs evolve in small communities. In time, some may coalesce or co-operate in forming national organizations or professional based groups. In recent years, international palliative care organizations have provided much needed support for many in the developing world in providing insight into the various aspects of a service program that is evolving in many forms around the world.

CULTURAL ISSUES

Because many palliative care and hospice programs were developed under the leadership and support of religious groups, palliative care is erroneously perceived by many as part of the Christian movement. The main concepts of palliative care: respect for the individual, compassionate care, holistic approach and the incorporation of the relatives and family members as part of the care team can be applied to all religions and faiths. The fact that palliative care programs and hospices have developed in many Islamic, Hindu and Buddhist places and regions of the World is an important indicator of the above. Although it is essential to recognize the role of spirituality in palliative care, it is unethical to take advantage of the emotional and physical fragility of a terminal patient to lure him into any faith other than the one he or she professes.

Individuals and families differ greatly from country to country in very sensitive issues such as the delivery of bad news, disclosure of the diagnosis, communication with the patient, patient autonomy and others. Perceptions and understanding of illness, death, bereavement and expressions of grief and bereavement vary across cultures and regions. Culture brings along much in the way of traditional beliefs as well as a conglomeration of rituals and taboos. Health care providers should be aware of the cultural differences that underline the communication quality and quantity between themselves and the patients. In the evolution of palliative care in developing countries, the pertinent influence of culture and religion needs to be continually considered in the same importance as the development of knowledge and skills in pain and symptom management.

Two aspects of cultural impact arise in the development and evolution of palliative care within the developing countries, especially those with a multicultural society. Palliative Care needs to develop clear guidelines and strategies in order to prevent misconceptions in care and concept. It needs to be an inherent part of the community rather than develop in ignorance of their perceptions. Failure to do so risks the possible non acceptance of palliative care by parts of the community.

In the search for appropriate healthcare systems to develop palliative care, many in developing countries may look and copy systems and structures in more 'developed' countries. The impact of this is often less than satisfactory. Developing countries need to be assisted in formulating systems pertinent to their needs. They require strategies in adapting care delivery systems, educational structures and advocacy skills to create the necessary environment conducive to growth in palliative care.

CONCLUSION

Health is a priority goal as well as a core issue in economic development and poverty reduction. Policy makers, analysts and economists and the international philanthropic community have underestimated the importance of investing in health. A few health conditions are responsible for a high proportion of the disease burden in the world: HIV/AIDS, Malaria, TB, cancer and childhood infectious diseases cause approximately 15 million deaths per year. More importantly, the HIV epidemic is killing individuals at the their time of most economic productivity, leaving behind children and elderly unable to provide, produce and care for themselves.

Significant changes are happening to the family structure in developing countries in addition to the staggering increase in the number of orphans in Africa. The majority of the population now resides in large metropolitan centers, many of them living below poverty level. Governments and policy makers need to ensure the availability of services in all models of care**.** Services must be tailored to the needs of the population and applicable to each, while anticipating the demand in different services. Developing countries will need to develop facilities capable of providing palliative care in order to avoid costly utilization of beds in hospitals as home care becomes more difficult to provide.

The level of health spending in low-income countries is insufficient to address the health challenges they face. The proportion of public spending in developing countries is approximately half of the cost of care, while in the developed countries is 70 percent. Governments in developed countries need to increase the amount of share for health care to ensure adequate access by increasing the domestic resources they mobilize for the health sector and use those resources more efficiently.

However, even with more efficient allocation and greater resource mobilization, the levels of funding necessary to cover essential services are far beyond the financial means of many low income countries as well a few middle income countries. Coordinated actions by the pharmaceutical industry, governments of high income countries, philanthropists, and international agencies are needed to ensure that the world's poor have access to essential medications and appropriate health care services, including palliative care. Palliative Care needs to be incorporated in the Public Health Care Policy to ensure its continuity and financial stability. Nations, individuals and policy makers should learn from the lessons of others that relief of unnecessary pain and suffering will contribute to a better quality of life for all.

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4 Ethical Issues in Palliative Care

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INTRODUCTION

Fundamental moral attitudes orienting the praxis of palliative care are the unconditional respect for the dignity of each human person, even in situations of extreme weakness and the acceptance of human finitude. The recognition of the needs of patients at the end of life demands some moral attitudes, skills and knowledge that enable an adequate decision-making in relation to the unique sources of suffering encountered in the dying and their relatives (1). "Simply stated, ethical issues in palliative care center around decisions which will enable us to satisfy the criteria for a peaceful death, dignified and assisted by a helpful society (2)." Hence, the application of some classical virtues and principles of medical ethics acquire special relevance in palliative care. These are mainly the virtue of truthfulness, compassion and prudence, and the ethical principles of respect for human life and death, therapeutic proportionality and double effect (in the administration of opiates or sedatives).

While the kind of ethical dilemmas most frequently faced by medical personnel in the care for the dying in the developing world does not substantially differ from the problems encountered in the developed world, there are some particular circumstances related to poverty, scarcity of medical resources, and cultural attitudes towards death and dying in the developing world that generate specific problems in the application of the classical ethical principles to concrete cases. Hence, more than different ethical principles, what is particularly needed in developing countries is the virtue of prudence, understood as practical wisdom. In fact, prudence plays a key role in disclosing the way in which the different classical ethical principles have to be applied in individual situations. In this chapter some of these classical ethical principles will be discussed and the way in which special circumstances in the developing world may interfere with their application in frequent ethical dilemmas in palliative care will be demonstrated.

ETHICAL PRINCIPLES RELEVANT TO PALLIATIVE CARE

The Principle of Respect for Human Life and Death

Life is a basic good from which other human rights can be derived. Indeed, life is a necessary condition for the exercise of all other human rights. Hence, the duty to respect and promote human life is the first ethical imperative in relation to the self as well as to the others. In palliative care the

ethical question raises as to how this basic ethical principle of respect for human life can be applied in the context of dying persons. Defining the specific goals of palliative care, the World Health Organization (3) states that "palliative care... affirms life and regards dying as a normal process,... neither hastens nor postpones death." This definition corresponds to a conception of the so-called 'right to die with dignity' not simply as a *right to die*, but rather as a *right to live one's life to the end*. In fact, there cannot be a 'right to die', but only a right to be assisted by others in the dying process. In other words, there is a *right to a specific way of dying*. The difference is extremely important, because it points to the concrete ethical challenges arising in the care for the dying. The main idea is that the human process of dying poses certain ethical demands for the medical personnel as well as for society as such. Palliative care is conceived as a concrete active answer to these ethical demands.

To answer the question about what constitutes an appropriate use of medical resources in the face of a dying person presupposes adopting a moral attitude towards imminent death and an understanding of the meaning of the so-called 'good death'. There seems to be general agreement about the fact that an artificially prolonged agony is contrary to the dignity of the dying person. The Judeo-Christian tradition, for instance, affirms the existence of a *moral duty to accept death* and regards the so-called 'medicalization of death' as an ethically wrong medical praxis, arguing that this is contrary to the dignity of the dying person and to the moral duty to accept death. But it is also well known that - in contradistinction to the way in which most proponents of euthanasia and medically assisted suicide understand the expression 'right to die with dignity' – the Judeo-Christian tradition absolutely excludes the possibility of intentionally taking ones own life and/or helping others to do so. In this conception, the *right to die* with dignity is considered as a constitutive part of the *right to live*.

These statements suggest the notion of a *good* and a *bad* death, in the moral sense of the expression. From an ethical point of view, to speak about a *good* or a *bad* death presupposes an understanding of the act of dying as an act in which human freedom can be exercised *(actus humanus)* – at least to a certain extent - and not as a merely involuntary act *(actus homini)* (i). In other words, the idea of the existence of a good and a bad way of dying rests on a conception of death as something that does not merely happen to us (mere passivity), but as an act that our free will is able to sanction (certain activity). Experience shows that death is not something we can decide about. We are not able to choose whether or not we want to die. But in spite of the inevitability of death proper to the human condition, we are actually free to choose an attitude of acceptance or rebellion in the face of imminent death. Doctor Elizabeth Kübler-Ross, for instance, describes five kinds of emotional reactions observed in patients facing death: anger, denial and isolation, pact or negotiation, depression and acceptance. The existence of various types of attitudes towards inevitable death suggests the possibility of a personal free choice in this regard: we are free to accept or to reject death. And it is precisely this inner attitude towards imminent death what becomes ethically relevant for a conception of a 'good' and a 'bad' death.

But one's view about what counts as a 'good' or a 'bad' death, is doubtless deeply influenced by the cultural and moral commitments one holds. Laín Entralgo sustains that death cannot be regarded as a primarily medical or scientific event. Death has a deep cultural, moral and religious meaning. Cultural, moral and religious views of death shape how it is understood and determine what is

considered as the appropriate behavior, both for the dying person and his or her family, as well as for the caring personnel. But health care is a cooperative enterprise that brings together people from different cultural and religious backgrounds. In the hospital, we die surrounded by people that have very different views of what a good life and a good death means. Thus, the orientation towards cure characterizing contemporary medicine may encourage aggressive treatment - even if not clinically appropriate and/or contrary to patient's wishes - in order to avoid any perception of undertreatment. To be involved by such a cultural trend, as well as by its opposite - i.e., the growing acceptance of the practice of euthanasia and physician-assisted suicide - may impose grave moral dilemmas on dying persons, not allowing them to die in the way the consider the right one. Indeed, surveys - like the SUPPORT study in 1995 - suggest that medical efforts to prolong life too often merely prolong dying, even against the explicit desires of patients. Although the study did not address the particular reasons why patients and/or their families rejected certain life-supporting measures, its results suggest that contemporary health care standards are not sensitive enough to the moral and religious dimensions that should shape our attitudes towards life and death. Health care workers too often fall into the temptation of using all available technology in order to avoid imminent death. They seem to have special difficulties in accepting human finitude and death.

There aren't any important cooperative studies like SUPPORT performed in developing countries in order to document current health care standards. However, in developing countries important differences exist between the diverse social-economic levels that usually coexist in these societies. Simplifying, the situation within the private health care institutions in developing countries does not essentially differ from the one observed in developed countries, in the sense that a legitimate desire to offer every opportunity for survival sometimes does not actually respect the moral duty to accept death and only increases suffering both for patients and their families. Moreover, it involves a strong investment of medical resources and the spending of an important part of the gross national product. In the public health care system the situation is quite different. The scarcity of resources may sometimes conduce to a kind of 'social euthanasia' in which non-terminally ill patients have to die because medical resources that would actually provide good chances for survival are simply not available. In this context, important clinical, ethical, financial as well as political questions arise. The question about justice in the allocation of scarce medical resources becomes extremely relevant. However, this important question falls beyond the scope of this chapter (ii).

The Principle of Therapeutic Proportionality

A fundamental moral intuition tells us about the existence of a moral obligation to preserve life and health. It is also evident that nobody is obliged to use all available medical interventions, but rather only those offering a reasonable benefit/risk ratio. A more difficult question is whether one can refuse medical interventions in spite of their potential benefits or accept treatments for which the risks are still very high or not yet well known. These situations confront us with the question about the limits of our moral obligation to pursue health.

In an attempt to distinguish morally obligatory from morally non-obligatory medical interventions, a conceptual distinction between 'ordinary' and 'extraordinary' means has been proposed. The content of this traditional moral teaching is presently better known as *principle of therapeutic proportionality*.

This principle states the moral obligation to provide a patient those treatments that fulfill a relation of due proportion between the employed means and the end pursued. Medical interventions in situations in which this relation does not hold, are considered 'disproportionate' (previously referred to as 'extraordinary') and regarded as morally non-obligatory (4).

This idea of proportionality in medical care has a long tradition. Already Plato emphasized the inappropriateness of medical efforts that result only in prolonging suffering. The conception that the goal of medicine is to help an organism affected by a *reversible* disease is an important heritage of Greek medicine. Greek physicians learned to recognize those situations in which a disease represented an obstacle to the realization of an otherwise healthy nature, from those situations in which nature was sick, leading human existence to its natural end. Thus, death was not considered as a failure of medicine, but as the natural end of human life. Indeed, Hippocratic medicine rejected efforts that were probabilistically unlikely to achieve a cure. So, both quantitative and qualitative aspects of medical futility are recognized in the ancient traditions and articulated today as principle of therapeutic proportionality. Medical interventions that do not fulfilling a relation of due proportion between means and results are considered 'disproportionate' and therefore morally non-obligatory.

In order to verify whether such a relation of due proportion holds in a particular case, one has to confront the type of therapy, the difficulties and risks involved in its application, the expenses, and the real possibility of implementation with the results that can be expected, taking also into account the patient's unique situation. It is important to note that to say that judgments about therapeutic proportionality are relative to an individual's unique situation is not equivalent to say that they are merely subjective judgments. In fact, in order to be legitimate, proportionality judgments need to be grounded on objective state of affairs regarding the clinical condition and the present state of medical art.

Some of the elements that need to be always taken into account in order to judge the proportionality of a given intervention are: the certainty of the diagnosis, the utility/futility of the intervention, the risks and side-effects of the different therapeutic alternatives, and the accuracy of the prognosis.

Even though a moral obligation cannot be sufficiently grounded on statistical probabilities, the application of statistical methodology – as suggested by so-called Evidence-Based Medicine – represents a useful tool in evaluating ethically relevant clinical information and establishing proportionality judgments. It seems prudent to ground our decisions on the most accurate possible knowledge of the objective state of affairs, specially in critical situations such as those associated with end-of-life decisions. But the empirically derived clinical information has to be analyzed in a larger decision-making framework, one that explicitly acknowledges the role of moral values in clinical decision-making.

In order to be able to judge the proportionality of a given medical intervention, one has to ideally reach a reasonable degree of certainty about the clinical diagnosis. A condition for any treatment is the previous identification of the symptoms and causes of the illness. Hence, the process of clarifying the diagnosis is commonly considered as an action promoting health and, therefore, morally good. There are situations in which the ethical dilemmas emerge precisely from having to make delicate

therapeutic decisions without being able to reach a reasonable diagnostic certainty. This might be the case in palliative care, where the need to control uncomfortable symptoms in order to support the patient's well-being takes priority over establishing the diagnosis.

It is important to distinguish these situations from those others in which physicians doubt about the proportionality of a given diagnostic and/or therapeutic interventions without having first sufficiently clarified the clinical condition, allowing themselves to be guided by the vague intuition of an ominous prognosis.

Patients have a right to any treatment from which they can draw benefits. The moral obligation to implement useful treatments refers not only to curative but also to palliative care. However, defining therapeutic utility is not an easy task. This concept has been widely explored in medical literature in the last years. An interesting conception of futility has been proposed by Caplan, who states: "medical futility must be understood as referring to both the probability and the desirability of attaining a particular diagnostic, therapeutic, or palliative goal" (5). So, a distinction between absolute, statistical and disproportionate futility can be made. *Absolute futility* refers to those completely ineffective interventions in physiological terms. Since there is a general agreement that a physician is not obliged to implement absolute futile measures, the limitation of this kind of therapies does not pose moral dilemmas. *Statistical futility* expresses a low probability of a specific measure to achieve a given goal. This information in itself does not say anything about the moral obligation to implement this measure. It represents morally relevant clinical information that needs to be considered in judging its proportionality. The expression disproportionate futility qualifies a value-laden decision to abstain from a certain medical intervention - in spite of its low statistical probability of achieving a beneficial therapeutic goal - because it is not justified in a given situation due to the sufferings, risks, costs, etc. it implies for the patient or his family.

Each medical intervention involves risks. The moral obligation to pursue health includes the duty to undergo only proportionate risks. Nobody is obliged to use a type of medical intervention which, although already in use, is still too dangerous or too burdensome. In such cases, a refusal is not equivalent to suicide. Rather, it may represent the acceptance of the human finite condition or the wish to avoid disproportionate interventions. In fact, the moral obligation to pursue proportionate health care is not defined by the strict utility of the interventions, but also by the feasibility and costs. It is important to understand the expression 'costs' in a broad sense, including not only financial aspects, but also other kind of burdens to patients, families and/or health care workers. These burdens may be physical, psychological, spiritual or familiar. So, a given medical intervention might be defined as partially useful, but judged as disproportionate in a concrete case, if it is too difficult to obtain, too burdensome, etc. This is not infrequently the case in developing countries, where medical resources are not always available, raising further ethical dilemmas related with the problem of social justice and solidarity in the allocation of scarce medical resources (iii).

Indeed, in developing countries health care reforms face important issues of priority and equity. The allocation of scarce medical resources has to be particularly efficient in order to ensure social justice. In the search for moral criteria orienting a just distribution of limited health resources, it

is important to keep in mind that the physician's primary commitment is to the patient. Thus, the physician should not argue on grounds of distributive justice in order to justify individual decisions to limit care. The very nature of patient-physician relationship does not allow that physicians limit medical interventions exclusively on financial costs. Unfortunately, in developing countries physicians are sometimes forced to make this kind of decisions, in fact limiting treatments they might consider necessary. Under these circumstances, a prudent discernment needs to be made in order not to become involved in a kind of 'social-euthanasia'. It is important to note that proportionality judgments are not the result of a mere cost/benefit equation. The way in which the different elements involved in therapeutic proportionality have to be weighted needs to be guided by the virtue of prudence. Wildes (6) states that: "Prudence, in contemporary philosophy, has come to mean the notion of rational self interest. However, ... the medieval understanding of prudence ... was ... the ability to be practically wise...the exercise of right choice in particular case, in light of moral universal knowledge... prudence was the knowledge of what should be done and avoided and it guided reasoning about what ought to be done." The moral relevance of judgments about therapeutic proportionality guided by the virtue of prudence is that the implementation of an intervention judged to be 'proportionate' is morally obligatory. To omit it would represent an act of euthanasia by omission (sometimes referred to as 'passive euthanasia').

The Principle of Double Effect in Pain Management and Sedation

The traditional principle of the double effect sheds light on various ethical problems that are frequent in palliative care. This principle sets the ethical criteria for the legitimacy of actions that have well-known, unavoidable bad side effects. There are, indeed, many situations in which one cannot do the good without also causing undesired bad side effects. This might be the case, for instance, when using opiates or sedatives in terminally ill patients, knowing that they may negatively affect the patient's blood pressure, respiration and state of awareness. Thus, the use of opiates and other drugs that affect the state of awareness of patients may raise ethical questions among patients, relatives and even among health care professionals, because they fear that the occurrence of adverse effects - like hypotension, respiratory depression, etc.- may hasten the patient's death, representing a form of euthanasia (sometimes referred to as 'indirect euthanasia'). This fear is not infrequent in developing countries.

In this context, it is important to remember first that an adequate use of this kind of drugs is not associated with the occurrence of such feared side effects. But even if the undesired effects would appear, the principle of double effect would help discerning the cases in which the use of these drugs may be morally legitimate. This principle states that actions with both good and bad effects are ethically legitimate only if certain conditions are simultaneously fulfilled:

1. *The action performed is not itself morally evil.*
2. *The good effect is not caused by the evil effect.*
3. *Only the good effects are directly intended; the bad effects are not intended but only tolerated (as unavoidable).*
4. *There is a due proportion between good and bad effects.*

Thus, the double effect doctrine forbids the achievement of good ends by wrong means. It forbids doctors to relieve the distress of a dying patient by killing him, but permits the use of drugs which relieve the distress of the dying, even when they may hasten death.

In order to understand the rationality of this principle it is important to keep in mind that the mere *physical* performance of an action does not necessarily coincide with a *moral* act. Only an action in which human freedom is exercised can be morally qualified. A moral act is essentially an act in which human freedom is exercised. This means that the moral act itself is marked by an 'intrinsic intentionality'; it tends towards an object (called *moral object*). Hence, the moral act cannot be properly characterized by describing a mere physical performance. In order to find out which is the kind of moral act we are performing (the 'moral species' of the act), the key question is: What are you doing? And an answer like "injecting morphine to this patient" would not do it. The proper answer to this question – "relieving pain" - revels the 'intrinsic intentionality' of the moral act as such. An analysis of the lived ethical experience shows that the moral character of our free acts is basically determined by the kind ('species') of act we perform.

But the ethical experience also shows that the agent's motivation does in fact play a fundamental role in determining the moral character of a given action as well. Thus, we have to add the question: Why (or for the sake of what) are you doing this? The answer to this question – in order to allow the patient to enjoy his life - will explain the actual intention or motivation of the agent inasmuch as it goes beyond the motivating role of the intrinsic intentionality of the act itself. Thus, the 'intrinsic intentionality' of the act itself and the intention of the agent are not the same thing and need to be carefully distinguished. A careful analysis of our most basic human moral experience shows that the ethical character of human acts does not primarily depend on the motivation or intention of the agent, but on the *moral species* of the action to be performed. Hence, the common saying 'the end does not justify the means'. The principle of double effect intends to secure that this necessary condition for the ethical legitimacy of our free actions will be respected.

If these concepts are applied to pain management with opiates, then what is actually intended is the control of pain - and not the reduction of blood pressure nor the depression of respiration- then the 'species' of act is analgesia and not euthanasia even though the side effects might unintentionally appear. Provided that other pain killers have been tried and shown as inefficient in the control of pain, and if the opiates are used in the right way and dose, then opiates would represent the only possible way of benefiting the patient and their use is therefore morally justified.

In the sedation terminally ill patients this principle applies analogously. If we consider the actual exercise of mental faculties to be a good for the person, then it would be morally not allowed to deprive someone from the use of these faculties without a sufficient reason. Hence, in order for sedation to be morally legitimate, the four conditions of the principle of double effect must be fulfilled. It would be morally wrong to sedate a person if there is not a good reason for it. Unfortunately, health care professionals are not always completely aware of the seriousness of this issue. So, in developing countries sometimes the scarcity of medical personnel and other related circumstances become the reason for sedating patients, which is a morally intolerable situation.

Truthfulness in Communication

Perhaps one of the most frequent ethical dilemmas in palliative care is the question of truthfulness with terminally ill patients. Reluctance to share the truth with the patient about his/her diagnosis or prognosis is frequently associated with family pressures and shows cultural differences. While medical professionals tend to think that by explaining the truth about diagnosis, prognosis, and treatment options to the patients the basis for freedom are generated, family members sometimes request to withhold the truth to their relatives. The main argument for such family requests to withhold the truth to the patient is usually the concern about the disclosure of diagnosis and prognosis being harmful to the patient. Hence, the apparently conflicting ethical principles in these cases are non-maleficence (or beneficence) and autonomy.

Non-maleficence and beneficence have traditionally been the leading principles of medical ethics. Hippocrates thought that the first ethical principle the medical profession had to keep in mind was 'do not harm' *(primum non nocere)*. Autonomy entered medical ethics much later, as part of a system of *prima facie*(iv) principles devised to deal with moral pluralism(v). The idea underlying the ethical principle of autonomy is that a person's freedom to make informed choices ought to be respected. While medical professionals usually consider truth disclosure to be part of their duty of beneficence and respect for autonomy, relatives sometimes regard truth disclosure as being harmful for the patient. Seemingly, what is beneficent for some appears to be maleficent for others. This contrast in moral perspectives underlies some ethical dilemmas arising in palliative care. Are family requests to withhold the truth about diagnosis and prognosis to a patient ethically acceptable? Should a physician respect a family's request not to disclosure a patient the truth about his or her diagnosis and prognosis? Does a family have a right to make such kind of requests? Can we simply say that the problem here is one of cultural and ethnic differences with regard to truth telling? What ought to be done if two or more of the prima facie principles conflict with each other? How can medical ethics help in solving this apparent value-confrontation?

A personalistic approach to medical ethics helps solving dilemmas related to truth disclosure to terminally ill cancer patients and their families (vi). It revels that the often-adduced conflict between non-maleficence/beneficence and autonomy with regard to truth telling originates from a narrow understanding of the concept of autonomy. This confrontation is, therefore, more apparent than real. From a personalistic perspective, truth telling goes far beyond providing mere information. Truth is not just the opposite of lie, not just the sum of correct statements, but a reciprocal state in the patient-physician relationship. In this context, deception appears to be harmful, because it may destroy the foundations of the interpersonal relationship that allows a doctor to 'do good' (beneficence). Thus, both respect for autonomy and truth telling can be regarded as intrinsic beneficent medical acts.

Usually, a family's request not to disclose the truth to the patients is based on the assumption that truth disclosure will induce serious anxiety and depression, causing a real harm to the patient. Indeed, detailed disclosure has been shown to increase anxiety in the short term. Follow-up reveals that the excess of anxiety dissipates within a few weeks, whereas the effects of limited information on psychological adjustment may persist. Evasion and lying isolate the patients behind either a wall of words or a wall of silence that prevents a therapeutic sharing of the patient's fears, anxieties, and other concerns.

If the physician believes that it is not possible to offer good care without a prior commitment to openness and honesty and goes on communicating the clinical information to the patient against the family's desire, he/she may be accused of an 'assault of truth', i.e., of imposing the truth to a patient. The risk thereby is to interfere with the patient's coping mechanisms, as determined by his/her personality or cultural background. In fact, we know that in the context of truth telling, in some ethnic groups the delegation of authority is culturally implicit. So, for instance in Egypt the cultural use is that the patient must be dependent and nurtured, and is not to be involved in decision-making. It is the family that makes decisions because dignity, identity and security are bounded by belonging to the family. Therefore disclosure of a serious diagnosis to a patient by the physician is socially unacceptable behavior and an untactful act. However, in this cultural medium the family has to be informed of the diagnosis and the plan of care. Egyptians also believe that it is the physician the one who has the education to treat the disease. Therefore, for them it would be impolite behavior to question or to interfere in the physician's work. In this cultural context an 'assault of truth' may cause an irreversible damage to the physician-patient as well as to the physician-family relationship. We encounter a similar situation in Latin American countries.

The uniformity of this cultural practice may suggest that delegation of decision-making to family members is an expectation of the sick person that does not need be made explicit in individual cases. This assumption cannot be taken for granted. The present trend towards globalization may result in a patient's appropriation of values different that the ones that are considered typical for his/her cultural background. One cannot just assume that a given patient will prefer one style to the other only because he or she belongs to a given culture or ethnic group. Thus, the physician should always tactfully explore the preferences of the individual patient with regard to communication and decision-making styles. The philosophical question underlying the ethical dilemma generated in such situations is the apparent dichotomy between holding to the existence of absolute and universal moral values – such as beneficence and respect for a patient's autonomy – and respecting the pluralism of different cultures. In other words, the challenging question is if bioethics is merely a 'cultural artifact' such that a universal medical ethics is not viable and we will have to accept that the only possible solution is an 'ethics of accommodation' as been suggested by some authors. I think that a personalistic approach to clinical ethics is capable of revealing that the confrontation between objectivism and cultural relativism in such situations is only apparent. A critical reexamination of the personalistic foundation and the meaning of autonomy shows that the dilemma derives from a narrow interpretation of the concept of autonomy.

Pellegrino (7) states that:

> *"the principle of autonomy is grounded in respect for the person and the acknowledgment that as rational beings we have the unique capability to make reasoned choices. Through these choices we plan and live lives for which we are morally accountable. Inhibiting and individual's capability to make these choices is a violation of his or her integrity as a person and thus a maleficent act. Autonomy, therefore, is not in fundamental opposition with beneficence as too often supposed, but in congruence with it. ... Autonomous patients are free to use their autonomy as they see fit – even to delegate it when this fits ... or find themselves unable or unwilling to cope with choices. Such patients may feel sincerely that a close friend or family member would be able to make decisions that better protect their values that they could make themselves. Such a delegation of decision-making authority may be explicit or implicit depending on the dominating ethos."*

In other words, there are different styles of decision-making that can be – in principle – equally respectful for patient's autonomy. One may be referred to as patient-based model, and the other one as family-based style. Therefore, in order to respect the patient's autonomous choice it is mandatory to explore carefully his or her preferences with regard to communication and decision-making. Hence, if a patient expresses the desire for a personal involvement in the decision-making process, he/she has the right to be informed in spite of the explicit requests of his relatives, who in such a case would be actually violating the patient's right to autonomy.

To state that competent human beings are owed the freedom to choose the communication and decision-making style they prefer, and to define beneficence in terms of their own values, is not equivalent to saying that all values are morally equivalent or defensible, nor than physicians are mere servants of patient's desires. What is actually affirmed is that as human beings we are owed respect for the choices we voluntarily make. But this applies obviously both for patients as well as for health care providers. Thus, if a patient or a family requests a path of actions that clearly violates the standards of care, the professional ethos or the law, the attending physician is free to reject the request, provided he or she will not abandon the patient.

For an action to be morally good not only the act itself (the 'what') and the reason for doing it (the 'why') have to be good; also the circumstances (the 'how') play a central role. In other words, to solve an ethical dilemma means not only to suggest that something ought to be done, and the reasons for it, but also to analyze which would be the best way of implementing the proposed solution. Thus, if in the context of truth communication we suggest that the ethical solution varies according to the patient's free choice with regard to the communication and decision-making style, we would have to examine an adequate way of finding out which these preferences actually are. A suitable way for doing it is to 'offer the truth' to the patient. The adequate timing of such an inquiry is also ethically relevant. If one would ask a patient if and how much he/she wants to know about the clinical situation right after significant tests have been performed, the patient will probably assume that the results are bad. Therefore, a physician should ask this kind of questions when he/she first gets to know a new patient, or – at least – before ordering any clinically significant test.

There are also other circumstances related to truth telling that are ethically relevant. This is the case, for instance, with the place and moment of the disclosure. Significant clinical information should be provided in at atmosphere of privacy and with the necessary psychological support. Thus, an important ethical challenge for doctors is to equip themselves with good, sensitive communication skills.

Summing up, a personalistic approach shows that the confrontation between beneficence and autonomy often stressed with regard to truth-telling in the context of terminally ill patients – especially if they belong to different cultures or ethnic groups - proves to be more apparent than real. In spite of cultural and ethnic diversities, autonomy can still be said to be valid and universal principle in relation to truth disclosure because it is based on what it is to be a person and in the respect due to each person as a person. What actually varies among different ethnic groups and cultures is the way in which the respect for a person's freedom is best exercised: the communication and decision-making styles. As in our days patients transplanted to other cultures for health care is

more common due to globalization, to preserve both autonomy and beneficence, physicians must get to know their patients well enough to discern when, and if, those patients wish to know about their clinical condition, as well as the communication and decision-making style they prefer. Personalistic ethics provides good insights for dealing with cultural and personal differences between patients and health care professionals.

TOWARDS A PERSONALISTIC VIRTUE-ETHICS FOR PALLIATIVE CARE

In an era of medical progress, in which the 'technological imperative' suggests that everything that is technologically possible is also ethically legitimate or –even more – ethically mandatory, the criteria for deciding what constitutes an appropriate use of high tech medicine cannot be driven from the logic of strict physiological utility. In caring for terminally ill patients, the logic of dominion - characterizing the process of technological progress - needs to be replaced by a 'personalistic' logic(vii). The physician's duty to maintain the dignity of the person and to respect the uniqueness of each person involves both the moral duty to implement proportionate treatments and the moral obligation to accept death. The peculiar characteristics of palliative care patients demand from health care workers – even more explicitly than in other areas of medicine – some fundamental moral attitudes or virtues securing the ethical dimension of the persons' life and death. These basic attitudes are an unconditional respect for the dignity of each person and the acceptance of human finitude. Thus, in order to discover what is appropriate palliative care "a physician shall be dedicated to providing competent medical services with compassion and respect for human dignity" (8).

This statement summarizes three central virtues in the praxis of palliative care: 1) medical expertise, 2) compassion, and 3) respect for the dignity of the person, even in situations of extreme debility and sufferings. Moreover, it is precisely a truly compassionate attitude what allows health care professionals to identify the concrete way in which medical expertise needs to be applied in order to actually respect the dignity of each person, specially in situations of unavoidable death.
The term 'compassion' is today commonly understood as synonymous of pity which is not the way it is used here. Dougherty & Purtilo (9), rather defined it as:

> *"the virtue by which we have a sympathetic consciousness of sharing the distress and suffering of another person and on that basis are inclined to offer assistance in alleviating and/or living through that suffering. Hence, there are two key elements in defining compassion: 1) an ability and willingness to enter into another's situation deeply enough to gain knowledge of the person's experience of suffering; and 2) a virtue characterized by the desire to alleviate the person's suffering or, if that is not possible, to be support by living through it vicariously."*

Compassion – understood as a moral virtue - is thus directed primarily to the person and secondarily to her sufferings. Since it entails the willingness to effectively alleviate a person's sufferings, it demands to unfold the corresponding expertise ('knowing how'). And it is evident that human sufferings have many different sources. Under this perspective, those medical interventions able to benefit a terminally ill person cannot be narrowly understood as those having the potential to produce certain physiological effects on the person's body, which is doubtless an important goal of care. But the medical commitment towards a suffering person reaches far more than her body. And in the context palliative care a peculiar source of human suffering is the person's natural fear of imminent

death. Thus, health care workers should develop a special sensitivity towards these aspects, permitting their patients to reflect on their moral duty to accept death and to receive the necessary psychological and spiritual assistance, if they want. This will require – among other things – to preserve the patient's state of consciousness, as long as the clinical condition and the therapeutic goals allow it.

If it is true that compassion is primarily directed to the person in virtue of her sufferings, and only secondarily to her sufferings – as said above – then, we can draw further practical conclusions. In situations of extreme and prolonged sufferings a truly compassionate attitude will prevent health care providers from the temptation of accelerating death in order to alleviate their patient's sufferings. To eliminate a person cannot be an act of true compassion, because such an act would eliminate the very object of compassion: the person. On the contrary, a compassionate attitude discloses health care providers the way in which their competent medical knowledge can be best used to palliate the person's sufferings in a way that truly respects each person's life and dignity, even in the events surrounding an unavoidable death.

CONCLUSION

The fundamental moral attitudes orienting the contemporary praxis of palliative care are an unconditional respect for the dignity of each person – even in situations of extreme weakness – and the acceptance of human finitude. Such a personalistic approach to palliative care provides the clue for overcoming the contemporary logic of the so-called 'technological imperative'. Although these reflections refer mainly to the process of individual decision-making ('micro-ethics'), they may have also some implications for institutional ethics ('inter-ethics') and even for society ('macro-ethics'). In fact, palliative care should be held to the same standards of excellence in all countries or in all regions of a country. It is known that the scarcity of economic and medical resources in developing societies often govern the kind of care that is actually provided. It may happen that there are variations in access to and differences in standards of palliative care from country to country and within any country. It is important to establish a minimum of excellence that ensures the respect do the each person's life and dignity. The principle of distributive justice demands that we seek the morally correct distribution of benefits and burdens in society.

Footnotes

i The classical moral distinction between physical and moral acts, is also expressed by the terms actus homini and actus humanus. The physical realization of an act (actus homini) does not necessarily coincide with the realization of a moral act. Only an action in which human freedom is exercised (actus humanus) can be morally qualified.

ii The interested reader will find helpful insights related to distributive justice in the allocation of scarce medical resources in a book edited by Cherry (2002), mainly in the chapters written by Wildes and by Boyle (5).

iii Please refer to a book edited by Cherry (2002), mainly to the chapters written by Wildes and by Boyle (5).

iv Prima facie is the Latin for 'at a first look'. In this context, the expression refers to moral obligations that are self-evident and need no further foundation or explanation in order to be accepted as truth.

v Prima facie principles in medical praxis, such as non-maleficence, beneficence, autonomy and justice, are those that ought to be respected unless powerful reasons for overriding them can be adduced.

vi According to a personalistic approach, the core of moral reasoning is derived from the fact that the proper addressee for a person as a subject of moral action is not duty as duty, or law as law (as has been proposed by other ethical trends) but a concrete, real person, who – in virtue of her dignity and ontologic structure - defines for every other person the field of her moral duty. We discover and fulfill ourselves as persons only when we affirm others as persons. Whenever we betray the respect due to another person, we betray simultaneously ourselves. In other words, our responsibility towards others converges with the responsibility towards ourselves. The 'personalistic principle' proposed by the Polish Personalistic Ethics School is "Persona est affirmanda propter seipsam et propter dignitatem suam" (Styczen, 1981)

vii The 'personalist principle' proposed by the Polish Ethics School says that the person shall be affirmed because of her dignity ("Persona est affirmanda propter seipsam et propter dignitatem suam"). Cf. Styczen T, 1981.

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5 Grief and Bereavement in the Developing World

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INTRODUCTION

The label "developing country" is an economic classification, which groups widely diverse populations. Therefore, any discussion on grief and bereavement needs to acknowledge the many variations in the conditions that exist within these nations in terms of democratic stability, economic viability, transport networks, health and welfare systems.

In this chapter we briefly discuss a few of the well known bereavement models and their applicability to grief and bereavement in developing countries, speaking mainly from experience in Zimbabwe. We detail the specific challenges faced by grievers in the developing world and outline some low cost interventions.

MODELS OF GRIEF

People's reactions to loss are as different as fingerprints. It therefore goes without saying that no one will fit neatly into any model of grief, although certain themes of grief do have a degree of consistency.

It is generally accepted that bereavement is an active process through which mourners pass over a period of time while they struggle to adapt and cope with their changed reality, both internal and external. Many models have been developed in the western world to help understand the process of bereavement. The earlier models tended to be more linear (Kubler- Ross's (1) clearly marked 5 stages) and to emphasize the "letting go" of the deceased (Bowlby (2)). Worden (3) and Rando (4) defined tasks to be completed, both culminating in the re-investing of emotional energy.

In 1996 Klass, Silverman and Nickman (5) edited Continuing Bonds which challenged the idea, that the purpose of grief and mourning is to cut bonds with the deceased, thereby freeing the survivor to reinvest in new relationships. Any idea of holding on to the deceased had been regarded as unhealthy. Writings by some of the most respected authors in the field of bereavement supported this emerging belief that the healthy resolution of grief enables one to maintain a continuing bond with the deceased. The bereaved find places for the deceased in their ongoing lives and communities. This idea fits well in cultures with beliefs in the continuing presence and intercession of deceased ancestors in a family's daily life – a very real continuing bond.

Stroebe and Schut in 1999 (6) refined their model of adaptive coping with bereavement, the Dual Process Model. They distinguished two types of stressors:

Loss oriented – involving the emotional processing of the loss; and

Restoration oriented – dealing with the many life changes and new roles that are brought about by the death

Healthy adaptation requires oscillation between these stressors. They proposed a dynamic coping process of moving between the emotional grief work, and practical life adjustments.

This is one of the reasons why this Oscillation model has appeal in the context of the tasks facing the bereaved in the developing world. In our experience it fits well with the fact that the bereaved have to continue to earn a living, cope with extended family and the myriad of life's daily challenges. As with trauma in traumatic grief, survival issues take priority over grief.

Grieving, whilst regarded as a painful yet normal and healthy process with its individually determined path, often proceeds for the bereaved in developing countries with a number of extra challenges. The additional difficulties that impact on the bereaved in developing countries are derived from four main areas:

- *Political*
- *Economic*
- *Social, Cultural and Spiritual Issues*
- *Other particular/specific challenges*

POLITICAL

In many developing countries, political instability results in varying degrees of turmoil and disruption of life for the population. Added to this reality is the concept that death can be politicized. In particularly unstable nations, political murders, disappearances and abductions do occur. These may or may not be policed efficiently as the systems of law and order may be unwilling to intervene or be unequal to the task. Should the deceased/disappeared be seen as in opposition to the community or powers that be, the bereaved person's need for justice may be thwarted. Disenfranchised grief may ensue. Doka (7), introduced the concept of disenfranchised grief where the social environment dictates the level of support to be offered following a loss. The grief may not be adequately recognized, the griever not acknowledged, and may in fact be eager to escape notice. During times of armed conflict the collecting of one's dead from the streets may risk identifying the allegiance of the bereaved. This can raise difficult ethical dilemmas vis-à-vis honoring one's dead versus keeping a low profile. Funerals themselves can be politicized exposing the mourners to possible retribution. The trauma surrounding the loss may cause the bereaved to put their grief "on hold" whilst they cope with personal and family safety and trauma issues.

In the case of abductions and disappearances, whilst the death of the victim may be suspected, lack of confirmation of death can create intense emotional difficulties. Beginning the grieving process when the person may still be alive is extremely difficult and distressing, and may seem disloyal, almost like a "giving up", especially in populations where talking about a person as dead whilst still

alive is taboo. Where no body is ever found and not available for burial, the required rituals may not be performed resulting in unfinished business for the surviving descendants. Situations have been documented (Argentina, Chile and Zimbabwe) where years after political killings, families have returned to find remains and bury or rebury what they can in order to heal and transform the living.

The Shona people of Zimbabwe believe that when the spirit passes into the next world it exercises tremendous power and influence. Every dead person must be properly buried according to appropriate rituals and procedures. If this is not done, they cannot be welcomed into the "Nyikadzimu" or spirit world and the "Ngozi" or spirit may cause the family grave problems until this is resolved. Although a western model of grief may label a family's pain and misfortune unresolved grief, the survivors themselves might talk of "Ngozi" (vengeful spirits) (8).

In addition during times of political turmoil certain places may become "no go" areas. This causes problems where the people need to travel to visit sick relatives, fetch and transport the body of the deceased, and attend funerals.

Compounding these problems, issues of power influence governments' willingness to accept help from civic institutions, e.g. non governmental organizations (NGO's) that move in to fill the void left by inadequate government systems. A wise government may be relieved to avail themselves of these or, conversely, may regard them with suspicion, and try to sabotage the efforts of the NGO's trying to provide these services, creating difficulties that hamper their service delivery to those who need them.

ECONOMIC

Economic factors such as rampant inflation, unemployment, low wages, currency devaluation and shortages test the endurance of the whole population in general and have a particular impact on the ability to respond to grief.

With the increase in economic refugees leaving developing countries, hospitals, clinics, psychological services and health and welfare support institutions suffer the loss of professionals and become understaffed, overworked, demoralized and burnt out. When services become pressurized it appears that health professionals neglect the emotional segment of the public need (9).

Whilst it is generally acknowledged that a certain degree of stress or "stretch" is stimulating and in fact possibly productive, these high levels of base line stressors that are experienced by palliative and bereavement care providers in the developing world exceed this boundary.

In countries with limited resources, bereavement counseling services can be seen as a luxury and not a priority. The counselor and the bereaved client have somehow to fill the gaps left by dysfunctional governmental structures that should be integral parts of the care continuum, e.g., feeding schemes that are not usually the preserve of a bereavement service, become essential. Shortages of basic foods clearly distract the bereaved from any emotional processing. "I am too hungry to grieve and my children are starving."

With high inflation rates and frequent currency devaluation, these developing countries often have limited or expensive resources. If a loved one dies in pain, or unnecessarily, due to unavailability or high cost of medication, this will cause the bereaved additional emotional pain.

The inability of a family to pay a medical account can lead to a hospital mortuary refusing to release the body for burial. Mortuary conditions themselves are affected by a country's economic downturn with power cuts and lack of maintenance of refrigeration services. In addition, increased deaths due to AIDS can cause overcrowding of facilities. Bereaved clients recount stories of the trauma and distress in identifying relatives in overcrowded, inefficient mortuaries.

Transport expense and shortages deny the poor the options of accessing health facilities for the sick, paying respects to the dying, attending funerals and offering family support. Funerals often take place in distant rural home areas. Acquiring the transport necessary to convey the body and the family is onerous and expensive. The whole funeral commitment is time consuming, causing problems for the mourners, who must retain any employment they may be lucky enough to hold.
A clear change has come about in some societies in the provision of food at funerals. Where once it would have been unheard of not to provide plenty of food for all mourners, now it is accepted that this is no longer possible.

An unresearched observation in Zimbabwe, which has experienced rapid economic deterioration in the last few years, is the flow of people back to their rural homes from urban areas. This is possibly based on the premise that economic survival is easier in terms of subsistence farming, significantly reduced transport costs, extended family support for patients, widows and orphans, availability of food aid and even burial costs. The terminally ill may choose to return to their rural homes to die in order to lessen the burden of their care. However, this does not release the rest of the family from the obligation to travel and incur the expense in order to attend the funeral and any subsequent milestone rituals.

SOCIAL, CULTURAL AND SPIRITUAL ISSUES

In many developing countries society is structured around the extended families that are used as resources. Whilst this financial, practical and emotional family support is ostensibly available, there are a number of factors that threaten this traditional approach. The toll of daily hardships may render family members less able to help than they would wish. The family structure, already evolving due to urbanization and modernization, has been dramatically altered in those countries most affected by the AIDS pandemic, with family size considerably reduced.

Urbanization has led to families living far apart. Distance, economic hardship, family deaths too numerous to mourn, community losses, constant funeral costs and frequent and extended time away from employment all contribute to bereavement overload for the entire family. A survey demonstrated that over 30% of Street kids in Zimbabwe identified "orphanhood" as their reason for being a street kid (10).

Economic constraints lead to only an ever-diminishing few bearing the burdens of the family. Hence, one will find that the "richer" family members (possibly merely those that have paid employment) are constantly called upon to contribute financially.

In an extended family system, attending a family member's funeral is culturally, spiritually and socially of great significance. In countries where individuals work, often illegally, outside their home country due to economic pressures, they may not be able to attend funerals, causing distress and hindering the grief process. Conversely, if a death occurs outside the country, great efforts are made to bring the body home for burial. In a belief system where the dead intercede for the living, the importance of completing the appropriate rituals is essential to the well being of the whole family. Families will incur huge debts rather than fail to repatriate their kin for burial.

In Zimbabwe the Shona believe that all misfortune, illness and untimely death are caused by malevolent forces, either from within the family (ancestral displeasure) or by active witchcraft. Therefore, particular rituals have to be performed during the bereavement period in order to ensure family well being of current members and future generations. As multiple generations or branches of a family may have different belief systems, with younger people tending to be more influenced by Christianity, this may lead to disagreements among family members about, for example, the use of traditional healers.

In reality, it is often the widow who is blamed for her husband's death. She may then be denied family support for herself and her children and may be ostracized and abandoned. Cultural practices concerning the distribution of the deceased's property often discriminate against the widow, leaving her with nothing. Her focus necessarily becomes survival, rather than grief work.

Changing ways and attitudes mean that practices originally intended to support the bereaved widow and children (e.g. In Zimbabwe inheritance of the widow by the deceased's brother) have begun to be questioned by some. Modern women want to choose their own partners and both men and women may be aware of the dangers of HIV infection.

Traditional societies with clearly defined mourning procedures leave little room for variation. This may be helpful in as much as the bereaved knows what is expected from them, and the community knows how to offer support. However, it becomes problematic when what is expected does not "fit" with how the bereaved feels or wants to behave. For example, in the Shona society of Zimbabwe, the mother is not allowed to attend the burial of a baby, which will be a simple affair in a pot near a river. She will be discouraged from grieving, rather being encouraged to have another baby. This may be unhelpful for her in her grief process.

If we are to help the bereaved, it is very important not to make assumptions about how they are feeling. In order to stimulate thinking along these lines, Hunt (11) developed a training tool, the "9-cell bereavement table", where trainees are challenged to think about how they themselves responded to loss in their own lives and how this matched with what society expected of them. This

is a useful tool, both for trainers from the same cultural background (who may be tempted to assume they know how their client's feel) and for trainers who know very little of the culture of the people they wish to help. This tool is applicable across all cultures.

OTHER SPECIFIC CHALLENGES

In developing countries the huge impact of the AIDS pandemic, and deaths due to illnesses that may be curable in the developing world, has to be noted and faced.

HIV/AIDS

Whilst a chapter in this book (See Chapter 10) is entirely devoted to HIV/AIDS, in the context of grief and bereavement the extent of the pandemic and its impact on certain populations has to be mentioned in order to plan adequately for bereavement care. According to UNAIDS.org, some of the front-runners in the HIV infection rates are South Africa, Zimbabwe, Botswana and Zambia.

By far the worst affected region, sub-Saharan Africa is now home to 29.4 million people living with HIV/AIDS. Approximately 3.5 million new infections occurred there in 2002, while the epidemic claimed the lives of an estimated 2.4 million Africans in the past year. Ten million young people (aged 15-24) and almost 3 million children under 15 are now living with HIV (www.unaids.org) as seen in Table 1 below.

Table 1 – Number of People Currently Living with HIV/AIDS in Selected African Countries

AIDS Statistics (End 2001)	Botswana	Zambia	Zimbabwe
Adults	300 000	1 000 000	2 000 000
Children	28 000	150 000	240 000
Women	170 000	590 000	1 200 000
Deaths	26 000	120 000	200 000
Orphans	69 000	570 000	780 000
Adult infection rate	39%	20%	35%

Source (UNAIDS) www.unaids.org

With the phenomenal death rate in countries with high HIV infection rates, and low availability of Highly Active Antiretroviral Therapies (HAART's), the number of orphans has inevitably increased and is cause for great concern.
Within Sub Saharan Africa UNAIDS estimated:

- *the number of orphans in Zimbabwe at the end of 2001 at 780,000 and 570,000 in Zambia;*
- *by 2010 AIDS will account for 48% of the deaths that leave children orphaned in Africa;*
- *The Zimbabwe National Aids Coordination Program estimates that 900 000 children will have lost their mother due to AIDS by 2005.*
- *Life expectancy estimates in most of Sub Saharan Africa has fallen to below 40.*

The deaths of young adults affect society in a particular way. In an agrarian society, families depend on the young, strong members to support the older generation. Bereavement issues in these circumstances include the practical "who will take care of us". Not only this, but the older generation finds itself having to take care of their orphaned grand children. The practical difficulties – economic shortages, physical limitations of age – are so overwhelming that they often inhibit grief and overshadow the emotional issues. These may include huge resentment at having to take on child rearing responsibilities they thought were over, which may be expressed by abusive behavior towards the children in their care. At times siblings will be separated and cared for by different family members, adding further devastating losses for the children to cope with.

This brings us to possibly the most damaging effect of the deaths of young adults – the impact on the children struggling to survive the death of one or both of their parents. More than 14 million children have lost one or both parents to the HIV/AIDS epidemic worldwide (12). By far the greatest number of these children is from sub-Saharan Africa. Children are the most vulnerable bereaved group, partly because of their relative lack of coping skills and the fact that children often "mark time" until an adult helps them with their grieving. With the extended family decimated by AIDS there are often no adults around to help with this process, and in particular the memory work so necessary for the child's sense of family belonging.

UNICEF chief Carol Bellamy (13) states, "Almost without exception, children orphaned by AIDS are marginalized, stigmatized, malnourished, uneducated and psychologically damaged. They are affected by actions over which they have no control and in which they had no part. They deal with the most traumas, face the most dangerous threats and have the least protection. And because of this, they too are very likely to become HIV-positive".

Many of these children who have nursed dying parents and siblings now find themselves as head of the "household" and are possibly themselves infected with the HIV virus. Whilst they may well be streetwise and practiced in the art of daily survival, they are emotionally underdeveloped in terms of future relationships and unable to contribute meaningfully to the economic development of the country. If Worden (14) found that children who had lost one parent were more "at risk" for high levels of emotional and behavioral difficulties than non-bereaved children, what might this mean if the initial loss is compounded by the death of a second parent and numerous family members? Worden also found that children, who failed adequately to mourn, often presented in later life with symptoms of depression, or the inability to form close relationships during their adult years.

An adult infected with HIV, as well as coping with their own impending death, may have infected their children through vertical transmission. Where a child has already died, guilt may be a grief issue with which to grapple. When they realize they will predecease the infected child, they face the agony of knowing their child must die without them.

Stigmatization of families who have experienced the death of a member through AIDS remains a real problem and may lead to community support being withheld. Noerine Kaleeba (15), Community Mobilization Adviser at UNAIDS, has this to say; "many countries in Africa are still riding on the wave

of fear, stigma, isolation and rejection, while others are moving slowly into the wave of awareness. But it is only a few, such as Uganda, that have moved into the wave of tolerance, solidarity and acceptance. It is this that we must strive for."

The spread of the virus through sexual intercourse often leads to judgments concerning promiscuity and an attitude that the illness is a deserved punishment. Governments, the health system and churches may compound the problem by silence, the use of confusing euphemisms when talking to patients, and denial. These attitudes can be isolating for bereaved families who fear talking openly of their loss.

UNEXPECTED DEATHS

In developing countries where access to the health system is limited, late diagnosis often means that what would be an expected death in the developed world is a sudden death in the developing world (e.g. cancer/AIDS).

Sudden, unexpected, and untimely deaths are more likely to be associated with difficult outcomes than are anticipated deaths, although death from slow terminal illness may also in some cases lead to difficult outcomes (16).

The differences between expected and sudden deaths are well documented and some of these are seen in Table 2 below.

Table 2 – Differences in Responses between Expected and Sudden Deaths

Expected	Sudden
Anticipatory grieving possible	No time to say goodbye
Unfinished business attended to	Many possible regrets
Varying levels of acceptance of inevitability of death	Shock – more time needed for Worden's 1st and 3rd tasks of mourning[4]
Future preparations possible e.g. finances, care of children	Family thrown into disarray
Exhaustion due to long-term care - Did we do enough?	

In Zimbabwe, and reportedly in many other countries in Africa, there is reluctance on the part of the medical fraternity to impart news of the life threatening nature of illnesses such as cancer and HIV/AIDS, and indeed of the diagnosis. Euphemisms that cloud the facts are often used e.g. "tumor", "immuno-suppressed" or "new serology." An unsophisticated, disempowered population is easily put off asking questions. This is one of a number of factors that limit opportunities to prepare for a death. Lack of access to health care and adequate medication, either through unavailability or poverty, results in deaths from illnesses that are curable or preventable in the developed world, such as malaria, gastroenteritis and measles.

In a developed country, death from a curable illness leads to acute regrets and often self blame in a family. In countries where these illnesses are often life-threatening people may be more fatalistic. However being to unable to access the treatments that cure, is a cause of burn out for doctors and nurses.

This lack of access to adequate health care also means a different age profile, with a greater number of younger people and children dying. The death of a child is a particularly devastating loss, leading to complicated, long-lasting grief.

SUSTAINABLE INITIATIVES

In developing countries the first level of help is the extended family and community. It is important to use the strengths of the family system, which solves problems as a group. Traditional counseling involves all community members so that everybody- brothers, sisters, uncles, aunts, grandparents and village elders – all provide help.

Communities with a strong extended family system have tended to resist discussing personal problems with outsiders. However with the fragmentation of the extended family outside assistance including counseling has become more acceptable.

There is an increasing number of emerging community initiatives, attempting to mobilize available resources to care for the bereaved, and these need support and capacity building. Improved collaboration and coordination between these service providers minimizes overlap and maximizes resources. Very often amongst these providers there exists the opportunity for cross training and service complementation if only networking and communication were improved.

NGO's in developing countries rely heavily on external donor funding which can be tenuous. Often when a donor has identified a program with integrity and of relevance to their particular focus, an ongoing financial relationship will be formed. What is clear is that the most sustainable interventions are those that are identified by a community as meeting a need, and use some form of community volunteer participation. Whilst donors have the financial resources, those in the field understand the local context and have the necessary experience.

Training has become the identified tool by which to reach as many of the bereaved in a community as possible. The cascade effect of bereavement skills training for health professionals or "bereavement counselors", whether in hospitals or clinics, home based care groups or community based organizations (often volunteers living with HIV/AIDS (LWHA), is expected to produce an improvement in bereavement care in the population. Training of trainers programs, provided they are efficiently planned, implemented and evaluated ensure greater dissemination of knowledge. As with all training programs, constant evaluation and retraining is essential, particularly in sub-Saharan Africa where high staff turnover exists due to migration and AIDS' deaths.

Medical staff often influences the first step in the bereavement process, and assisting them to be aware of how to help rather than hinder the process is essential.

A survey by Island Hospice and Bereavement Service (17) in 1999 of existing bereavement support systems in High Density Areas in Zimbabwe recommended that "it appears more time and cost-efficient to better utilize already existing bereavement support systems in this community". It suggested that specialized bereavement counseling training could improve any existing support services e.g. churches and burial societies, and endorsed grief awareness and education for the community.

Recent comparative research by Hunt (9) of palliative and bereavement care services in India and Zimbabwe seems to support the premise that the most sustainable, low cost interventions utilize the concept of volunteer harnessing in the community and the raising of public and professional awareness of the needs of the bereaved.

According to Hunt (9)"The findings of this research identify the most workable combination for the provision of macro palliative care to be a "top down" (state driven) *and* a "bottom up" (community driven) approach as suggested by Stjernsward and Clark" (18).

Hunt's research identifies that physical comfort is prioritized in palliative care in both India and Zimbabwe and that emotional and spiritual support is usually left to the family. The views of her respondents indicated little evidence that health policies commit to developing counseling resources.

As mentioned under the political heading, governments may not have the economic ability or political will to implement these top down health policies in order to augment NGO's committed to developing better palliative and bereavement care services to the community. This is unfortunate, as it does appear that having a strong civil society is a key element in fighting the AIDS epidemic. The adult HIV infection rate in Senegal, a country that mobilized most elements of society, is around 1%, compared with infection rates well above 25% in some other African countries. It is concluded that strong community institutions and sustained volunteer efforts do help stem the spread of this disease.

One example of a cost effective model of care has been developed by Zimbabwe's Island Hospice & Bereavement Service (Island). The first hospice in Africa, established in 1979, they have operated a comprehensive bereavement service since inception. Over the years Island has gradually adapted its service delivery to the terminally ill and bereaved to include a massive training program in home based palliative and bereavement care. The organization's training program reaches all sectors of the community, from anesthetists in intensive care units in urban hospitals, to rural community volunteers.

In Zimbabwe, partnerships have been developed between Island and various orphan care systems, including established children's homes and community groups where a high orphan population exists. A program that integrates a direct service for children, training for community volunteers working with children and support for the carers has been successful. Acknowledging the stress of caring for these often terminally ill children, whilst many of the carers are themselves HIV+ and most certainly bereaved, is an integral part of this program. Professional support and supervision is regarded as essential.

In spite of the overwhelming difficulties, many communities have come up with creative low cost ways to support the bereaved. The following examples of programs are taken from International HIV\AIDS Alliance (19). These programs are adaptable to a variety of settings and problems.

The Community–based Options for Protection and Empowerment (COPE) program in Malawi has helped communities set up village orphan committees. Village committees are linked to agricultural extension agents, who provide advice for the communal gardens that produce food for vulnerable families and revenue to finance committee activities.

In Zimbabwe, the Families, Orphans and Children under Stress (FOCUS) program gives volunteers basic training to identify and register orphans in the community, to recognize those in need of help, make regular visits and provide material and practical support to enable children to remain in their homes and communities.

The Chikankata Community Health and Development Team in Zambia runs a similar program, using teachers, community health workers and village leaders.

In Zimbabwe, the Farm Orphan Support Trust (FOST) developed a program where children who cannot live with family, live in small group homes integrated into their own communities. They either live with a paid guardian or in adolescent–headed households that are visited regularly by a member of the community childcare committee.

Whilst understanding the overwhelming workload and challenges that face health workers coping with distressed and bereaved people, it should be remembered by all who practice in these countries, that the most essential and lowest cost intervention should be compassion. This can be offered free and will have a lasting impact on the recipient.

Of course, the cheapest intervention is prevention! Educating communities, and specifically, health workers and home based care workers in ways to talk more openly about death allows for anticipatory grieving to be done and practical preparations to be made.

Workbooks adapted appropriately for different populations, and memory books or boxes can encourage family communication and leave the bereaved with a concrete reminder of their roots. In the NACWOLA project in Uganda, while parents are still alive, they encourage their children to visit and socialize with as many relatives as possible so that they get to know their extended family well. Bonds are strengthened to promote a sense of belonging in the children.

Identifying vulnerable families and mobilizing help as soon as possible will minimize negative consequences of loss. The following have been identified as useful indicators:

- *families with large numbers of children*
- *poor economic capacity of carers*
- *presence of sick children*
- *child-headed households*
- *grandparent-headed households*
- *single-parent headed households*

Although female-headed households tend to be more vulnerable economically, a study in Uganda showed that children living with single, male parents suffered the most neglect (19).

CONCLUSION

It is clearly apparent that the bereaved in the developing world are at risk of being overwhelmed by secondary stressors and difficult life circumstances. This can result in a bias towards "restoration" type activities with insufficient loss oriented or emotional processing. Without this emotional processing only partial healing can take place.

The resilience of communities is demonstrated by innovative programs, which deserve support. In dealing with the challenges that add to the burden of organizing and implementing services, it is necessary to use any available resources as wisely and effectively as possible, remembering that each country's situation is unique.

Western countries have proposed and published most of the bereavement theories. In response to the very different conditions in the developing world it is expected that new research, emanating from those countries, will challenge some of these widely accepted western theories.

APPENDIX 1 - GRIEF MODELS
JOHN BOWLBY (1969-80) (2)

Emanating from his studies of maternal deprivation, Bowlby looked at how attachments influence our interpersonal relationships. He believes that grief is a form of separation anxiety.

According to Bowlby, grief is set in motion when the bereaved observe that the object of their affection or attachment no longer exists. The pressure to withdraw the energy from the deceased in order to re-invest in new relationships may be resisted. The bereaved may deny the reality of the separation (death) and attempt to retain the attachment to the deceased. His model of "working through" the grief is continual reality testing until the energy is gradually released, and the attachment broken. In all but his latest publications, Bowlby appeared to define grief resolution in terms of the severing of bonds with no room for the idea of a continuing relationship with the deceased.

Bowlby believed that grief is an adaptive response to loss
The reality of the loss must be confronted and accepted
Grieving is an active process and takes time

ELIZABETH KUBLER-ROSS (1)

Kubler Ross outlined 5 phases patients go through when coping with dying. Accepting the concept of anticipatory grieving,(i.e. the losses faced before the actual death) these have also been used to explain grief.

Stage 1 Denial and Isolation
Stage 2 Anger
Stage 3 Bargaining
Stage 4 Depression
Stage 5 Acceptance

WILLIAM WORDEN (1982) (3)

Worden's grief model specifies four tasks that the bereaved must complete in order to reconcile their grief.

1. *Accept the reality of the loss.*
2. *Work through the pain of grief, experience the pain of loss. This pain is physical, emotional and spiritual. The avoidance of this pain prolongs the course of mourning.*
3. *Adjust to a life without the deceased Developing the skills needed to cope with life's new demands, and taking on new and often unwanted roles*
4. *Emotionally relocating the deceased and moving on with life, Reinvesting in a "new reality", withdrawing the emotional energy that had been invested in the relationship with the deceased and re-focusing this.*

THERESE RANDO (1984) (4)

The "*6 R Processes*" model portrays the grief process as consisting of six individual but interacting processes

R*ecognize the loss - acknowledge the death*

R*eact to the separation of the loss - experience the pain and express the emotions*

R*ecollect and re-experience all the feelings involved including the negative aspects of the relationship with the deceased*

R*elinquish attachments to the deceased and the old world.*

R*eadjust to the 'new world' without forgetting the deceased.*

R*e-invest the 'freed up' energy in a new life or identity.*

Although not strictly speaking a model, the next group of authors developed a new understanding of grief.

DENNIS KLASS, PHYLLIS SILVERMAN, STEVEN NICKMAN, (1996) (5)

In 1996 these authors edited Continuing Bonds. New Understanding of Grief, which challenged the idea that the purpose of grief and mourning is to cut bonds with the deceased, thereby freeing the survivor to reinvest in new relationships. Any idea of holding on to the deceased had been regarded as unhealthy. Writings by some of the most respected authors in the field of bereavement supported this emerging belief that the healthy resolution of grief enables one to maintain a continuing bond with the deceased. The bereaved find places for the deceased in their ongoing lives and communities

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6 Cancer in Developing Countries

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INTRODUCTION

According to the World Health Organization (WHO), by 2005 sixty percent of the cases of cancer will occur in the part of the world that has only 5% of the world resources to fight the disease (1). The reasons are mainly economic: lack of financial resources to buy drugs and develop cancer centers and the non-existence of programs to foster prevention and early diagnosis. In developing countries, cancer strikes approximately 5,000,000 people annually, and little is known about their characteristics and lifestyles (1).

The purpose of this chapter is to describe the main cancer-related diseases, their prognosis, occurrence and oncological and adjuvant treatments available. Specific treatments will be analyzed taking into account the limited financial means available in developing countries.

Because the lack of availability and access to diagnosis, pathology resources and cancer centers, the overwhelming majority of cancer patients in the developing world are diagnosed at advanced stages of diseases (80%). All of them will benefit from effective palliative medicine, but only a minority will get a partial response to oncological treatments (2).

INEQUALITIES AND CANCER RISK FACTORS

In many developed countries, there has been a decline in the incidence of lung cancer parallel to a reduction in tobacco consumption. Screening programs, healthier diets and the use of preventive drugs will possibly help reduce the incidence of some cancers. However, as life expectancy is extended, the risk of cancer increases in steadily aging populations. It is estimated that the most frequently occurring cancer in the future will be prostate cancer, followed by breast cancer. Although the increasing occurrence of some cancers will be unavoidable, it is hoped that new molecular-targeted therapies together with improved knowledge in genetics and cancer plus advances in imaging will produce a decline in the death rates in developing countries (3).

Cancer experts are less optimistic about the current and future situation in developing countries. Tobacco companies have targeted developing countries as new markets for their products which implies an increasing number of tobacco-associated deaths. Globalization is also a contributory factor in cancer etiology as people in developing countries have adopted unhealthy Western habits

such as alcoholism, highly caloric diets rich in red meat and low in fiber combined with low physical activity. Since there are limited or non-existent official campaigns in these countries to increase public awareness on healthy dietary habits as a means of cancer prevention, the incidence of cancers such as colon, esophagus and breast is dramatically increasing. Since vaccination programs for infections that play a role in cancer etiology are still not available in most of the developing countries, carcinoma of the liver, associated with hepatitis B, is one of the most frequent cancers in these regions.

Cervical cancer has been virtually eradicated in some Nordic countries thanks to screening programs. Unfortunately, in developing countries, screening is too expensive and cervical cancer has a high occurrence rate.

Current problems of developing countries can be summarized as follows: lack of prevention, inadequate screening programs for early diagnosis, and limited access to cancer treatments. These problems need to be addressed using available resources in a rational and fair manner by focusing on four cancer control strategies: Prevention; Early Detection; Active Care of potentially curable tumors using specific antineoplastic treatments where there is a promise of an improvement in the quality of life and survival; and finally Palliative Care to improve the quality of life of patients and their families suffering with far advanced, incurable, cancer.

Table 1 shows the five most common cancers in developed and developing nations (1).

Table 1 – Annual Incidence of the Five Most Common Cancers (1)

	Male	Female
Developed Nations (in thousands)		
Breast	--	579
Lung	471	175
Prostate	415	--
Colorectal	319	291
Stomach	208	125
Developing Nations (in thousands)		
Breast	--	471
Lung	431	161
Cervix Uteri	--	379
Liver	325	132
Stomach	350	192

WORLD HEALTH ORGANIZATION CANCER CONTROL PROGRAM

The World Health Organization (WHO) has established a model for a National Cancer Control Program for countries that includes these four components for an effective intervention in cancer care (4). This program has been widely disseminated and partially adopted by several countries. However, many National Cancer Control Programs do not have all four components and governments need to take the necessary measures in order for these to be adopted by health institutions, cancer care centers, community centers and hospitals.

Cancer Prevention

Prevention means eliminating, or minimizing, exposure to the causes of cancer. It is this approach that offers the greatest public health potential and the most cost-effective long-term cancer control. Tobacco use in all forms is responsible for about 30% of all cancer death in developed countries, and this percentage is rising in developing countries. It is responsible for 80-90% of all lung cancer deaths and a great percentage of the deaths from cancer of the oral cavity, larynx, esophagus and stomach (5). The habit of tobacco chewing in some Asian countries is associated with oral cancer. Various strategies have demonstrated that it is possible to reduce tobacco consumption thus preventing a percentage of cancer.

Scientific evidence suggests that about one-third of the cancer deaths that occur in the USA each year are due to nutrition and physical activity factors, including obesity. There is a link between overweight and several types of cancer such esophagus, colorectal, breast, endometrium and kidney. Some recommendations are: limit the consumption of read meats, especially high fat and processed meats, choose whole grains in preference to processed (refined) grains and sugar, and eat several servings of vegetables and fruit each day.

There is strong evidence that healthful dietary patterns, in combination with regular physical excercise are needed to maintain a healthful body weight and to reduce cancer risk. Another aspect of diet clearly related to cancer risk is the high consumption of alcoholic beverages, that convincingly increases the risk of cancer of the oral cavity, pharynx, esophagus, liver and breast.

Occupational and environmental exposure to a number of chemicals can cause a variety of cancers: lung cancer (asbestos), bladder cancer (aniline dyes), and leukemia (benzene). Some infections are related to certain types of cancer: viral hepatitis B and C cause cancer of the liver, human papilloma infection cause cervical cancer; Helicobacter pylori increase the risk of some kinds of gastric cancer. Exposure to ionizing radiation is known to give rise to certain cancers, and excessive solar ultraviolet radiation increases the risk of all types of skin cancer (3).

National policies should be enacted to reduce exposure to these risks and governments should enforce the adoption of preventive interventions.

Early Detection

Early detection comprises early diagnosis in symptomatic populations and screening in asymptomatic, but at risk, populations. With early detection it is possible to cure some cancers: breast, cervix, colon and rectum, mouth, larynx and skin. It is critical that people are taught to recognize early warning

signs of the disease and seek prompt medical attention: lumps, sores that do not heal, abnormal bleeding, persistent indigestion, and chronic hoarseness. Screening is another approach to early detection in an asymptomatic population at risk. There is no doubt about the benefit of the screening for cervical cancer for all women that are sexually active or who are 18 and older. Women aged over 50 should have an annual mammogram and clinical breast examination and should perform monthly breast self-examination.

Diagnosis and Treatment of Cancer

A correct diagnosis is necessary and includes diagnostic studies (endoscopy, imaging, histopathology, cytology and laboratory studies) followed by staging of the cancer in order to establish a prognosis and therapy.

The treatment of cancer is decided according to two main factors:

1. *The microscopic characteristics of the tumor as found in a biopsy; and*
2. *The anatomic distribution of the tumor. The most common system for staging cancers according to anatomic distribution is the* ***Tumor, Nodes, Metastasis (TNM)*** *system. The* ***T*** *stages cancers from* ***I*** *(minimal size tumor, usually with no involved modes and no metastasis) to* ***IV*** *(usually large, unresectable tumor).* ***N*** *expresses the level of involvement of lymph nodes (****N1*** *for local nodes) to* ***N2*** *and* ***N3*** *(reginal and/or distant lymph nodes).* ***M*** *expresses the presence of distant metastasis.*

Some cancers such as,hematological malignancies and pediatric tumors have special stating systems that are beyond the content of this chapter anf publication. Staging of melanomas is described in the melanoma section in this chapter.

Treatment may involve surgery, chemotherapy, hormonotherapy, radiation therapy, or some combination of these. Optimal treatment of people diagnosed with certain types of cancer detected early, for example, uterine cervix and corpus, breast, testis, and melanoma, will result in 5 year survival rates of 75% or more (6). By contrast, survival rates in patients with cancer of the pancreas, liver, stomach, and lung are generally less than 15% (6).

Potentially Curable Tumors

The majority of early stage solid tumors are potentially curable with surgery, which in some cases may be combined by adjuvant treatments. This is why early diagnosis through screening tests should be promoted among the general public. Standard screening methods include PAP smears, mammograms, colonoscopies and PSA tests.

Individuals should see a doctor when some symptoms develop such as change in bowel or bladder habits, bleeding, nagging cough, and hoarseness, growth of a node or changes in color or size of a cutaneous nevus.

Most solid tumors in advanced stages in adults are not curable, with the exception of testicular cancer (seminoma and non-seminoma) in men, extragonadal germ cell tumors, trophoblastic tumors and ovarian germ cell tumor in women.

The following tumors generally occur in young adults and have good chances of cure with standard chemotherapy treatments, even in advanced stages with metastatic spreading:

Undifferentiated carcinoma: when a young adult develops a retroperitoneal mass, a mediastinal mass or lung nodes, and biopsy states undifferentiated carcinoma, it is vital to rule out the presence of a potentially curable cancer (germ cell cancer or lymphoma). Immunohistochemical techniques and serological markers (BHCG, AFP and LDH) can be used.

Lymphomas: Hodgkin's disease is a hematological tumor which presents a favorable global prognosis of more than 75% when treated with standard chemotherapy patterns MOPP (Mechlorethamine, Oncovin, Procarbazine, Prednisone) and ABDV (Adriamycin, Bleomycin, Vinblastine, Dacarbazine) and/or radiotherapy, depending on the disease staging (6).

Non-Hodgkin's Lymphomas having intermediate and high level of malignancy are neoplasms derived from B or Y lymphocytes. Though rapidly mortal when untreated, they have a prognosis of nearly 50% if they respond to treatment. The first line treatment is CHOP (CYCLOPHOSPHAMIDE, DOXORUBICINE HCL, ONCOVIN, PREDNISONE), combining drugs of relatively low cost (like in the case of Hodgkin's disease).

Non-Hodgkin's lymphomas having low level of malignancy: tumors in stages I (only one lymph node site involved) and II (more than one lymph node site involved in the same side of the diaphragm) are potentially curable with radiotherapy.

Indolent or low-malignancy lymphomas are generally diagnosed in stage III (disease spread to both sides of diaphragm) or stage IV (visceral hematogenous involvement plus frequent bone marrow involvement). Although these tumors are not generally curable with standard chemotherapy combinations CVP (CYCLOPHOSPHAMIDE, VINCRISTINE, PREDNISONE) and C-MOPP (CYCLOPHOSPHAMIDE, VINCRISTINE, PROCARBAZINE, PREDNISONE), treatment can provide long-term remission, with an overall survival rate of 7 years.

Palliative Care

Palliative care is a component of the WHO Cancer Control Program. It improves the quality of life of patients and their families facing the problems associated with life-threatening illness, by limiting and preventing suffering associated with the progression of the disease. It involves the early identification, assessment and treatment of pain and other physical, psychosocial and spiritual symptoms.

With adequate palliative care, following the recommendations developed by WHO, it is possible to relieve cancer pain in about 90% of patients (see Chapter 8 of this publication), improve quality of life for the patients and their families and reduce the over utilization of health care services (2). In addition, palliative care is the most effective approach in treating advanced cancer and is applicable in all cancers in all stages of the disease. Table 2, page 73, summarizes the applicability of Prevention, Early Detection, Curative Treatment and Palliative Care in the eight most common cancers. Palliative care can be provided relatively simple and inexpensively, and should be available in every country.

Table 2 - Cancer Control- priorities and strategies for the eight most common cancers (2)				
Site	**Primary Prevention**	**Early Diagnosis**	**Curative Treatment (*)**	**Palliative Care**
Stomach	+	-	-	++
Lung	++	-	-	++
Breast	-	++	++	++
Colon/Rectum	+	+	+	++
Cervix	+	++	++	++
Mouth/Pharynx	++	++	++	++
Oesophagus	-	-	-	++
Liver	++	-	-	++

*Curative for majority of cases with a realistic chance of early diagnosis

Key: ++ effective + partly effective - not effective

SYMPTOM MANAGEMENT

The following are some of the common symptoms and problems which may occur in advanced cancer and require immediate attention. Other symptoms and conditions are described in the cancer site subsections further in the chapter.

Spinal Cord Compression: It's considered an emergency in oncology. Spinal cord compression occurs in 5% of cancer patients, and more frequently in patients diagnosed with lung, breast and prostate tumors. In most cases it develops after metastasis to the vertebrae. The most common place of the compression is the dorsal area (80% of the cases) and a simple X-ray can show lesions to the vertebrae or a collapse at some level. If available, an MRI is the best way to confirm it. Whether the patient will be able to recover or remain paraplegic depends on a rapid diagnosis and prompt treatment. Health care professionals should always suspect spinal cord compression in cancer patients who develop parestesia and/or paresia of lower limbs or some loss in sphincter control. The emergency approach within the 24 hours of diagnosis is the use of corticosteroids (dexametasone 24 to 100 mg/day) and spinal cord decompression with radiation therapy or decompressive laminectomy.

Superior Cava Vein Syndrome: It can also be an oncological urgency, as it may threaten the life of the patient. It occurs when there is tumoral compression on the superior cava vein by primary or secondary tumors of the mediastine: cancer of lung, lymphomas or germinal tumors. Symptoms include edema in the head, neck and supraclavicular regions, cyanosis in the face and upper limbs, dyspnea, nausea, drowsiness and convulsions. Treatment with corticosteroids, radiation therapy and addition of chemotherapy in chemo sensitive tumors, such as small cell lung cancer, can be effective.

Hemorrhages: Hemorrhage is rare. If massive hemorrhage occurs, this can be a stressful situation for the patient and his/her family. The digestive hemorrhage is the most common one, most of the

time as a result of esophageal varicose veins or gastritis by NSAIDS administered for pain treatment. A massive pulmonary hemorrhage can be the result of an erosion of a greater vessel by carcinoma of the lung. Hematuria is very common in patients with bladder cancer and may occur occasionally in patients with kidney cancer, but in very rare cases it ends in an emergency situation. The priority treatment in potentially fatal, massive hemorrhages in terminally ill patients will be sedation, preferably with midazolam at 5-10 mg sc or iv, titrating the dose until the desired level of sedation is obtained. Dark, red or green towels and bacinets are an effective and simple way to disguise the contrast of blood on white sheets and in that way, prevent additional stress for the patient and the family. The decision to transfer the patient to an emergency room or an ICU depends on the place and the magnitude of the hemorrhage, the patient's overall condition, the possibility to continue domiciliary care and of the patient's life expectancy.

Uterine and Vaginal Hemorrhage: Frequently, endometrial, uterine and cervical cancers present some vaginal bleeding. In the case of advanced or recessive tumors, a larger hemorrhage may occur which will require emergency care. The initial management of acute hemorrhage should be the application of compresses. Radiation therapy can also be effective in controlling hemorrhage, by using either external or intracavitary therapy. In cases in which radical pelvic radiation therapy had already been applied, is possible to re-irradiate with a dose ranging from 8 to 20 Gy in one to five fractions.

Pressure Ulcers: Nearly 10% of hospitalized inpatients develop bed sores. The frequency is greater in patients with cancer due to the association of the following risk factors: immobility as a result of weakness, pain, sedation, massive ascitis and coma. Malnutrition, dehydration and anemia also predispose the apparition of bed sores. Lack of sphincter control will result in fecal and urinary incontinence which dampen the skin and increase the chances of developing a bed sore. When ulcers progress, they tend to become infected with common germs or Gram (-) bacteria. The treatment of bed sores should be focused on diminishing the source of skin irritation through adequate hygiene by cleaning any urine, sweat or fecal matter in the pressure zones. Surgical debridement of the necrotic tissue should be done, infections should be treated with local antibiotics and the neighboring skin should be protected. The injuries that aren't necrotized or infected will need a dry environment that can be obtained with semi permeable dressings to facilitate granulation. Daily nursing care, including irrigation of saline solution, rotation of the patient, ventilation of the affected area, skin debridement and the use of semi occlusive dressings with or without antibiotics will help accelerate the healing of deeper ulcers.
At any rate, for a patient in agony, the healing of the sore should not the main objective, but rather measures of hygiene and adequate pain treatment to diminish the discomfort and suffering.

Hypercalcaemia: The association of hypercalcaemia to malignant tumors is frequent and occurs in 10-50% of advanced cancer. Causes include Paraneoplastic syndrome which result from the release of a peptide similar to PTH (PTHrP), an increase in the bone and intestinal re-absorption and a decrease in the renal excretion of calcium; Local osteoyithic factors from components secreted by tumor cells which produce bone re-absorption and bone metastasis.

Hypercalcaemia is a medical emergency and symptoms vary depending on the magnitude and onset of the disease. These include somnolence, delirium, polyuria, nausea, fatigue and constipation. Diagnosis is determined by the calcium levels (8.5-10.5 mg/dl).

Treatment: If the hypercalcaemia is mild or moderate: Parenteral hydration IV or SC with saline solution 100-120 cc/hour. If after 24 hours the hypercalcaemia persists, bisphosphonates such as Pamidronate IV or Clodronate IV or SC can be added. Newer, more expensive bisphosphonates include Ibandronate or Zoledronate.

Ascitis: The metastatic effect on the peritoneum occurs frequently. The types of cancer which originate peritoneal seeds are the digestive tumors (colon, stomach, pancreas) and tumors of the female genital tract (ovary and endometrial). Others include breast and lung cancer, sarcomas, lymphomas, leukemia and myelomas. Symptoms include ascitis, diffuse abdominal pain, anorexia and caquexia. Less frequent symptoms include nausea, vomit, and intestinal obstruction. Peritoneal carcinomatosis indicates advanced stage of the neoplasm and has a bad prognosis. Treatment should be focused on the reduction of ascitis and the discomfort that it generates. Paracentesis is very helpful and alleviates much of the abdominal discomfort. Diuretics are not effective in these patients, except if patients have edemas due to other causes. Surgery is indicated to palliate complications such as intestinal obstruction. In selected cases, good results have been obtained with different with intraperitoneal and systemic chemotherapy to eradicate perintoneal lesions and control the tumor and recurrences.

HEAD AND NECK CANCER

Head and neck cancer tumors are still an important health problem worldwide.

In 2003, five hundred thousand new cases of cancer will develop worldwide, and this disease will affect many regions in the third world. Nearly 90% of head and neck cancers are related to the exposure to carcinogenic substances, among which tobacco stands out (3). Other etiological factors are alcohol, virus, radiations, occupational exposures, diet and hereditary factors.

Etiology and Epidemiology

Tobacco and alcohol: The habit of smoking and chewing tobacco is dramatically increasing in third world countries, mainly in the young Asian countries, Latin America and some African regions (3).

Alcohol is also an important promoter of carcinogenesis per se, but many researchers claim that ethanol increases the effects of tobacco smoke. Patients with head and neck cancer who consume tobacco and alcohol may develop multiple unstable precancerous lesions, or second cancers, along the superior pulmonary and digestive tract plus they have independent risks of malignancy among various other sites.

Virus: Epstein/Barr virus infection is associated with nasopharyngeal cancer (3).

Biology

Most head and neck cancers are squamous cell carcinomas, from the most undifferentiated to the most differentiated. In the nasopharynx, non-keratizing and undifferentiated tumors develop into lymphoepitheliomas. The pre malignant lesions which result in these tumors are leukoplakia and erythroplasia (with histological features of hyperplasia or dysplasia). They can both result in invasive cancer, but erythroplasia implies a greater transformation risk.

Diagnosis and Staging

Head and neck tumors are generally diagnosed in men over 50 with a history of alcohol and tobacco consumption. Signs and symptoms at the moment of diagnosis widely vary according to localization of the primary tumor and the cancer stage.

Because of inadequate information and lack of access to dental and medical check-ups, a considerable part of the cancers in the developing world are diagnosed in advanced stages.

The most frequent signs and symptoms of nasopharyngeal cancer are nasal obstruction, epistaxis and changes in hearing. Neuropathies caused by cranial nerve compression and upper cervical adenopathies develop in advanced stages. Oral cavity tumors develop causing pain and non-healing ulcers.

Hoarseness can be the initial symptom in laryngeal cancer.

In general, signs and symptoms of any localization are pain, otalgia, air passage obstruction, cranial neuropathies, trismus, dysphagia, odynophagia, limited tongue mobility, fistulas, ocular symptoms and cervical adenopathies.

Malnutrition resulting from unhealthy dietary habits or symptoms such as odynophagia, trismus and difficulty in mastication are also frequent.

Staging is made on the basis of combined imaging methods like Computerized Tumography (CT) and Magnetic Resonance Imaging (MRI).

Treatment Options

Early Stages

Head and neck cancers (T1and T2) are treated with radiotherapy or resection. In the USA, 30% of patients are diagnosed in these stages; cure will result in more than 80% of patients in stage I and in nearly 60% of patients in stage II (10). In some regions, however, this rarely occurs.

Lack of modern radiotherapy equipment and lack of training of general practioners - who, in many cases are general surgeons, or throat surgeons- make local or regional failures rates high.

The prognosis for patients with locally or regionally advanced cancer (stages III and IV) is much worse. Most of these patients die soon as a consequence of persistent or recurrent tumor.

Treatment strategies for such cancers are extensive surgery and radiotherapy (sequentially used) or chemotherapy.

- *Nasopharynx: Nearly 60-90 of patients with nasopharingeal cancer develop node metastasis. Lymphoepitheliomas have a more favorable prognosis than squamos cell carcinomas. They are highly radiosensitive and Radio Therapy (RT) is the advocated treatment. Survival after 5 years is 37-62% and is influenced by the tumor stage and radiation techniques and doses used (6).*
- *Oral cavity: The most frequent tumors affect the floor of the mouth and tongue. The choice between surgery and radiotherapy depends in most cases on the functional effects anticipated by the treating General Practitioner (GP), the patient's general condition and the need of node dissection.*
- *Oropharynx: The most frequent neoplasms affect the tonsils and the floor of the tongue. Radiotherapy confers local management rates of 80% of the cases of tonsils tumors in stage T1 or T2 (11). Severe complications such as trismus occur in less than 10% of patients. For bigger tumors, radiotherapy is sometimes used to avoid functional aftereffects and potential disfigurement conditioned by the lower jawbone removal.*
- *Larynx: Radiotherapy is the most commonly used treatment in early stages of vocal cord cancer. Actuarial survival rates after radiotherapy are 96-98% in T1 and 80-94% in T2. More severe complications such as severe edema and chondronecrosis occur in less than 5% of patients (11).*
- *Cervical Nodes: Treatment of the neck depends mainly on the primary tumor management. If the primary treatment was surgery, an elective lymph node dissection is frequently used, which results in sub-clinical disease management in more than 90% of the cases (11). The rates of sub-clinical cervical tumors management with radiotherapy as primary treatment are similar to those reached with surgery. Management of clinically positive cervical nodes (N1-N3) is also related to primary tumor management.*

Recurrent or Metastatic Tumor

The aim of treatment of patients with recurrent or metastatic cancer is to reduce the tumor size and palliate pain through symptoms management. In these cases, most patients develop coexistent processes as a consequence of aging and of alcohol and tobacco abuse, which conditions the use of cytostatics. The standard drugs are methrotrexate, flourouracil and cisplatin (6).

Response rates depend on the tumor stage and the patient's general condition. Generally, 15-30% of patients have short-lasting responses when treated with drugs as single agents, which compare new drugs such as taxans + cisplatin + carboplatin with the standard regimen of fluorouracil-cisplatin.

Combined Therapies

Chemotherapy is superior to radiotherapy alone and should be accepted as standard treatment of patients with locally advanced head and neck cancers.

Quality of Life

The quality of life of patients with head and neck cancer is significantly altered both by the disease itself and by the treatments. In addition to difficulties in speech, swallowing breathing and pain,

alterations in family, social relations and depression are also major problems. Nearly all these problems have a chronic course and many of them are irreversible.

The problems resulting from each of the traditional methods are:

Side Effects of Standard Treatments

- *Surgery:* Disfigurement, voice loss, difficulty in chewing and\or swallowing, increased salivation, changes in taste.
- *Radiotherapy:* changes in taste, xerostomy, esophageal stenosis, osteoradionecrosis, and fibrosis in soft tissues, cervical contractions, facial edema, calcium deficiency, trismus, and hyperthyroidism.
- *Chemotherapy:* increased mucus production, infections, nausea and vomiting.

Supportive Treatment

The most frequent problems that arise from supportive treatment are:

Mucositis: mainly associated to chemotherapy treatments. Supportive measures include use of ice, local anesthetics and analgesics (generally opioids).

Xerostomia: caused mainly by radiotherapy, chemotherapy, certain drugs, dehydration, and oxygen therapy. Whenever possible, causes of this symptom should be treated. Standard measures include oral hygiene many times a day, supply of humidified oxygen, ice, vitamin C, lemon or pineapple sweets, and supply of artificial saliva. Pilocarpine used after radiotherapy has proved to reduce the dry mouth sensation but has no demonstrated effects in salivary secretion.

Infections: Candidiasis is the most frequent micotic infection. Local nystatin or antifungals like ketoconazol, itraconazol or fluconazol are highly effective.

Xerostomia, chemotherapy, radiotherapy and immunodepressants are responsible for bacterial infections to negative Gram germs. Treatment is based in the above-mentioned standard measures and on antibiotic therapy according to culture results.

Herpes simplex, cytomegalic virus, varicella Zoster virus and Epstein-Barr virus are the main viral infections. Topic or systemic acyclovir treatments are effective as long as leukocytic count is greater than 600 elements\mm3.

Neutropenic ulcers: treated with standard measures and antibiotics. Culture stimulating factors contribute to management by accelerating granulocytes recovery.

Halitosis: Nearly 80% of cases of halitosis are directly related to primary tumors (6). Doctors should recommend oral hygiene, smoking and alcohol cessation, systemic antibiotics (metronidazol) and dental treatment.

Sialorrea: Single or repeated dosages of hyoscine can be recommended.

ESOPHAGEAL CANCER

Esophageal cancer accounts for 1.9% of all cases of cancer in the USA and is the cause of the same percent of all cancer deaths as well (12). Its incidence has risen in the last decades parallel to a change in histology (increase in the number of adenocarcinomas over squamous cell carcinomas) and localization of the primary tumor (more tumors in the distal tubule).

Esophageal cancer is rarely diagnosed in people before 40 and age increases risk. It is three times more frequent in men and prevails in black people. Risk factors include alcoholism, tobacco (synergic effect), diet (i.e. high-nitrosamine diet) and presence of Barret's esophagus associated to gastroesophageal reflux (the last mentioned is strongly related to adenocarcinoma).

Esophageal neoplasm is rarely curable. The five-year survival rate for all patients with esophageal cancer is less than 10% and less of 20% patients are living 5 years after undergoing surgery with curative intent. Only 25% of patients are cured with surgery in early stages and the survival rate at five years for these patients is approximately 70%.

Clinically, 90% of patients present with progressive dysphagia, odynophagia, thoracic pain and general symptoms, 80% with weight loss (6). Diagnosis is made after an adequate clinical history and medical examination through standard chest X-ray and endoscopy plus biopsy. If possible, staging should be completed with a thoracic (CT). Effectiveness of ultrasenography has been demonstrated. The standard staging system is Tumor-Node-Metastasis (TNM) of ACJJ.

Fifty percent of this tumor occurs in the middle third, 30 to 40% in the lower esophagus and 10 to 20% in the upper esophagus. Less than 50% are squamous cell carcinomas and the rest include adenocarcinomas (12). Esophageal cancer has distant metastasis to adjacent organs (lymphatic spreading) and to regional lymph nodes (hematogenous spreading), 32% to the liver and 21% to the lungs.

Surgery is the procedure of choice in early stages, with a postoperative mortality of 6%, 40 to 60% morbidity and 20% of major complications.

Radiotherapy plus chemotherapy has been suggested as treatment option to surgery to avoid perioperatory mortality and palliate dysphagia. Randomized trials of combined therapy have proved improved quality of survival. A moderately economical choice is a weekly regimen of cisplatin (radiosensitizing) plus radiotherapy.

Nearly 50% of patients present with metastatic disease at diagnosis and are therefore candidates for palliative treatments(13). The main occurring symptom is dysphagia, and the approach will vary depending on the moment of emergence (at diagnosis or during treatment), staging (I-II-III-IV) and of the patient's performance status.

It is vital to encourage the patient and their families to take up healthy dietary habits, i.e. reduce dietary volume, and increase its frequency and process foods. In case of aphagia, enteral feeding by catheter or ostomies should be considered. The placement of endoesophageal tubes for feeding will depend on the patient's PS and the staging of the disease.

These treatments can also be pharmacologically supplemented with the use of steroids (to reduce peritumoral edema and increase the light diameter), anticholinergics (to reduce saliva secretion and the lower esophageal sphincter size), antimicotics (nystatine/ketoconazol to reduce candidiasis generally associated to the primary tumor).

GASTRIC CANCER

Gastric cancer ranks fourteenth in incidence in the USA (14). The etiology is unknown but acknowledged risk factors include: Helicobacter pylori, advanced age, male gender, diet including salted foods, atrophic gastritis, pernicious anemia, cigarette smoking and familiar polyposis.

The standard treatment option aiming at curative effects is radical surgery. Depending on the localization, patients may be candidates for distal subtotal gastrectomy or proximal subtotal or total gastrectomy, plus lymphadenoctomy (stages I, II, III and IV {M0}).

It has not yet been proved that radiotherapy or adjuvant chemotherapy alone prolongs survival. Patients with high chances of relapse after radical surgery (i.e. T3, t4, N1, 2,3, M0), the use of adjuvant chemotherapy has proved effective, with survival benefits (36 vs. 27 months), Overall Survival (OS) at 3 years (5% vs. 41%) and relapse-free time (48% vs. 31%) (14).

In stage IV (M1), different palliative chemotherapy regimens have been used. The most common regimens are based on fluorouracil, leucovorine, cisplatin and etoposide. Other treatment options include use of endoscopic laser and placement of scents to palliate obstructions and palliative radiotherapy to relieve pain, bleeding and obstructions.

Chronic Nausea: It is a common, unpleasant symptom in patients with advanced cancer, occurring in up to 70%-90% of these patients. Nausea is prevalent in patients with stomach, breast, or gynecological cancer (13).

The etiology of nausea is often multifactorial: drugs, metabolites and toxins may stimulate the chemoreceptor trigger zone, which in turn relays information to the vomiting center to induce nausea. The vomiting center receives ascending impulses from lower centers such as the gastrointestinal tract, pharynx, and serosa through the vagus, glosopharyngeal, and splanchnic nerves. It also receives descending impulses from cerebral cortex, thalamus, vestibular system. Important chemoreceptors and mechanoreceptors in the gastrointestinal tract and central nervous system have been identified. Pharmacological disruption of these receptors is the major target of antiemetic medications. The major neurotransmitters that interact with these receptors include dopamine, acetylcholine, serotonin, and histamine.

Management of chronic nausea: The underlying causes should be identified and treated when ever possible. These are: constipation (add fiber foods, stool softeners, etc to the diet); opioid toxicity (rotate opioids); raised intracranial pressure (use corticosteroids and/or irradiation); anxiety (explanation, reassurance anxiolytics); electrolyte imbalance, gastric or duodenal mucosal irritation (H2 antagonists); and hypercalcemia (use biphosphonates).

Pharmacological measures: The primary mechanism of opioid-induced nausea operates via dopaminergic receptors. Metoclopramide is the drug of choice because it has antidopaminergic action and also peripheral effect (improves gastric motility). Haloperidol is an important antidopaminergic drug. It is a good alternative for opioid-induced nausea and for complete bowel obstruction, which precludes use of metoclopramide. Ondansetron is a potent antiserotoninergic drug and is the best drug for chemotherapy-induced nausea. Hyoscine is a good choice for intestinal obstruction colic and for the secretions in bowel obstruction. Diphenydramine can be used in vestibular system-induced nausea.

PANCREATIC CANCER

Pancreatic cancer is the third most frequent cause of cancer death worldwide. Only 15 to 20% of patients have potentially resectable disease at diagnosis; the rest is locally advanced (unresectable or metastatic) (14).

For those patients with locally advanced disease, survival rate is 8 to 12 months without treatment. The use of chemotherapy plus radiotherapy provides a moderately improved quality of life in treated patients. Clinically it is often associated with epigastric pain, jaundice and abdominal tumorgenesis. An adequate surgical approach is essential. If the tumor is resectable, a total duodenopancreatectomy is recommended; if the tumor is unresectable, surgery may be offered as palliative treatment for pain, obstructive jaundice and duodenal obstruction. For resectable tumors treatment, the effectiveness of chemotherapy or adjuvant radiotherapy as single modalities has not yet been proved. In locally advanced tumors (with partial or total resection) postoperative chemotherapy may have some benefits over surgery alone.

Ninety percent of patients have pain, jaundice or both, which are classically associated to weight loss and psychiatric disorders. Pancreatic cancer is one of the most difficult to treat, with mortality rates as high as 95% (6). It presents as a polysymptomatic development which should be followed adequately, and periodically, to improve the quality of life of patient at all times.

COLON CANCER

Colon cancer is the third most frequent cancer in men and women and the third most common cause of cancer death in the USA. Risk factors include both hereditary and environmental factors.

Colon cancer incidence increases with age and is more common in men. The risk triples in case of family history (1st grade). Predisposition has been proved in patients with syndromes of familiar poliposis and multiple familiar polyposis, Gardner, Tucot and Olfield syndromes. Previous pathologies such as ulcerous colitis and Chron's disease also increase risk almost 20 times. The importance of high-fiber diets to reduce risk and prejudicial effects of high-fat and high-protein diets has been demonstrated.

Depending on the anatomic localization, colon cancer can present with abdominal pain, palpable mass, anemia, intestinal obstruction, constitutional symptoms or metastatic disease manifestations. Fifty two percent of tumors occur in the descending colon and sigmoid, 32% in the ascending colon and 16 in the transverse colon. It causes metastasis to adjacent structures or lymphatic spreading to regional nodes as well as hematogenous spreading to liver (60 to 70%), lungs (25 to 40%), bones (5 to 10%), ovaries (3 to 5%) and CNS (1%) (15).

Prognosis for colon cancer is directly related to the level of tumor spreading to the colon wall and the presence or absence of nodal involvement. Ninety eight percent of cancer cases are adenocarcinomas and staging is based in AJCC's TNM system. Dukes' staging and Asthler and Coller's modified system can also be used.

After diagnosis is done with the aid of clinic, lab tests, imaging (colon enema) and endoscopic exams, staging should then be completed with thoracic X-rays, abdominal and pelvic CT and carcinoembryonic antigen exams. Carcinoembryonic antigens are not essential for staging but are very useful for postoperative follow-up. Surgical resection of the primary tumor and of regional lymph nodes is the golden standard treatment.

In 1997 the American Society Clinical Oncology's guidelines recommended the use of regimens combining two or three drugs (flourouracil + leucovorin/flourouracil + levamisol, or flourouracil + leucovorin +levamisol) as adjuvant treatment as chemotherapy had clearly demonstrated benefits over surgery alone. This benefit is possible in patients in stage III (Dukes' C), whilst no statistical benefit is present in patients in stage II (Dukes' B).

In patients with metastatic tumor, stage IV (Dukes' D), standard combination was flourouracil + leucovorin, which was cross-examined against current regimens with oxaliplatin, irinotecan and capacitabine. Although these new drugs improved response and survival to a certain extent, colon cancer is not considered curable and all therapies should aim at improving quality of life.

RECTAL CANCER

The tumor is localized under the peritoneal reflection of the rectum or the lower margin is within 12 cm of the endoscopic anal margin. Adjuvant treatment in early stages is the same as in colon cancer plus radiotherapy aimed at reducing local recurrences, whose symptoms are generally difficult to palliate.

Intestinal Obstruction

Intestinal obstruction is a frequent clinical condition occurring in patients with advanced abdominal or pelvic cancer. Although the greater incidence results from ovarian cancer (42%), colon cancer causes 28 to 30% of its cases (14). It can develop as initial disease symptom or during unfavorable development of the pathology.

Treatment options will differ in both situations, from the NGS placement and surgical procedures in cases with no previous antecedents, to the use of medical treatment in advanced or terminal cases. In these patients the placement of nasogastric tubes will be avoided and surgical procedures will be

postponed and only considered in extreme cases. Medical treatment will be offered to improve the patient's quality of life.

Pharmacological Management:

- *Management: use of subcutaneous opiates (according to the WHO standards – see Chapter 8) in combination with adjuvant analgesics (NSAIDs and steroids).*
  Depending on whether the obstruction is partial or total patients may be offered prokinetic drugs such as metoclopramide or antispasmodics like hyoscine and atropine.

- *Nausea and vomiting: the use of certain drugs aims at the reduction of vomits to one or two times a day: metoclopramide (according to the level of obstruction), haloperidol (persistent obstruction) and steroids can be useful. Past studies have demonstrated the effectiveness of the use of octreotide; unfortunately, it is a very expensive drug. The option of gastrectomy (surgical or subcutaneous) should not be ruled out.*

Patients in terminal stages should be encouraged to eat and drink every kind of food they wish, especially favorite meals and drinks. If necessary, intermittent subcutaneous hydration should be recommended.

HEPATOCELLULAR CARCINOMA

It is a relatively infrequent disease in developed countries, with increasing incidence due to hepatitis C virus infections. It is potentially curable with total surgical resection, but this is the procedure of choice in a small number of patients.

It is associated to cirrhosis in 50 to 80% of cases, and it is frequently multifocal (6). Hepatitis B and C are the main causes of hepatocarcinoma in the world, although it has also been associated to other diet-related risk factors such as aflatoxins, peanuts and alcohol intake.

Clinically, 50 to 60% of patients present with hepatic mass (hepatomegaly) associated to general symptoms (6). Alphafetoprotein determination is of use for follow-up care; it increases in 75 to 90% of cases and falls to normal values after complete resection (6).

Even with the most advanced techniques in modern surgery, only 33% of patients with hepatocarcinomas are candidates for resection; thirty three percent of these (10 to 12%) can be totally resectable and 33% of the latter (3-4%) can have long term survival, usually 3 years (16). Resection must be decided on taking into account the patient's performance status, presence or absence of viral infection, presence or absence of cirrhosis and hepatic function.

Those patients with unresectable localized disease may be candidates for chemoembolization, cryosurgery, percutaneous ethanol injection or radiofrequency ablation (not available in non specialized centers). Prognosis is poor for all cases, with more chances for recovery in fibromatous or capsulated hepatocarcinoma with more than 25% of OS to 5 years (18). In patients with associated cirrhosis, OS to five years is zero, and resectable carcinomas, 5-year OS can reach 10 to 15% (6).

OVARIAN CANCER

Ovarian cancer has an annual incidence of 17/100,000 female population women, with an increasing incidence of 54/100,000 in patients over 75/79. The average age at diagnosis is 61. Most of the cases of ovarian cancer (70%) are diagnosed at advanced stages of the disease.

Risk Factors:

- *Hereditary factors or first grade family history.*
- *Nuliparity.*
- *BCRA 1-2 gene mutations: the risk is 16-40% whilst in general cases it is 1.73%.*

Favorable Prognosis Factors:

- *Early age*
- *Clear cells*
- *Early staging of disease*
- *Good PS*
- *Small residual tumor size*
- *Absence of ascitis*
- *BCRA 1 mutation*

Prevention:

Oral contraceptive pills (OCP): they reduce risks of ovarian cancer 11% each year they have been used till 50-70%. This may be due to annovulation and the effects of progesterone, which would produce apoptosis in the ovarian epithelium.

Retinoids: Fenretinide 200mg/day. Protective effects decrease if the drug is discontinued.

Detection Methods:

- *Annual gynecologic exam*
- *Pelvic ultrasound: 53% sensitivity; if doppler effect is added, CA -125 has a value minor to 10% as independent marker (17).*

Treatment Options:

- *Surgery: aiming at reducing the tumor mass*
- *First line treatment: cisplatin-paraclitaxel Response rate (RR): 73%*
- *Cisplatin/cyclophosphamide RR: 60%*

Differences in the cost between these two combinations are abysmal, thus cisplatin-cyclophosphamide regimens should be recommended in developing countries, even increasing cisplatin doses to 100mg/ms to increase response rates.

Other possible combinations having similar response -though more expensive- include:

- *carboplatin (AUC 6)- paclitaxel: less nephrotoxic, for patients with affected renal function*
- *carboplatin (AUC 6) -docetaxel: less neurotoxic, for patients with peripheral neuropathies such as diabetics*

Second line treatment:

- *Etoposide RR: 6-30%*
- *Gemcitabine RR: 13-19 %*
- *Paclitaxel RR:21-48%*
- *Doxorubicin liposomal RR: 20-26%*
- *Cisplatin RR: 21/-76%. If relapse occurs more than 6 months after completing the first line of cddp chemotherapy, the cycle can be repeated.*
- *Tamoxifen RR: 18%*
- *Topotecan RR: 13/20%*

Second line treatments should be considered palliative aiming at the patient's quality of life. Treatments will depend on the patient's PS and should be offered to alleviate symptoms with the least toxicity possible.

Common complications: generally intra abdominal.

- *Intestinal obstruction: treatment may be surgical (single obstruction site) or aiming at symptoms management (steroids, octreotride, antiemetics, ostomies).*
- *Ascites*
- *Hydronephrosis*

CERVICAL CANCER

In developing countries, cervical cancer ranks second in incidence. There are 470,000 new cases per year of cervical cancer and 231,000 deaths from it worldwide. Eighty percent of the cases occur in developing countries since screening programs are not effective and treatments are not early. Only 5% of women living in developing countries have screening tests done, contrasted to more than 50% of women in industrialized countries (3).

Risk Factors:

- *Multiple sexual partners*
- *First sexual intercourse under 16 years of age*
- *Sexual intercourse without protection*
- *Promiscuous partner*
- *Uncircumcised sexual partner*
- *Sexually transmitted diseases (STD): Human Papilloma Virus (HPV), Chlamydia, HSV-2, HIV*
- *Biological factors: smoking, immunosuppression, malnutrition*
- *Intra-uterus exposure to diethylstilbestrol*
- *OCP for over 5 years*
- *High parity*
- *Hereditary factors*
- *Socioeconomic factors: low socioeconomic level, lack of access to health system, rural residence, obesity*

Screening is recommended:

- *3 years after the first sexual relation*
- *for women over 21*
- *if the patient has a previous history of cervical cancer*
- *in cases of intra-uterus exposure to diethylstilbestrol*
- *in patients with immune compromised diseases (HIV+)*
- *in women over 30 with 3 consecutive negative Pap tests: they should have screening tests every 2-3 years*

Prevention of Cervical Cancer in Developing Countries

In places where Pap smears are not available because of lack of infrastructure and financial constraints, patients should have visual cervical inspections with acetic acid followed by immediate cryotherapy treatment when test results are positive.

Treatment Options

Early stages: local surgery with curative intention.

Advanced stages:

- *Radiotherapy-brachitherapy*
- *Chemotherapy: the standard drugs are cisplatin, isofamide and taxanes.*
- *Pelvic exeneration surgery*

All of these are palliative treatments.

Most frequent complications: obstructive hydronephrosis, bleeding, fistulas, intestinal obstruction.

ENDOMETRIAL CANCER

It has an annual incidence of 17/100,000, with an annual mortality rate 7/100,000. It is the fourth most common cancer in women. The majority of the cases are diagnosed in postmenopausal women (55/65 years of age) (6).

Symptoms develop early: metorrhagia (80-90%) and leukorrhea (10%). Seventy five percent of the cases are diagnosed in stage I (6).

Risk Factors:

- *Estrogen hormone replacement without progesterone*
- *Early menarche*
- *Late menopause*
- *Nuliparity*
- *Annovulation*
- *Estrogen-producing tumors*
- *Diabetes*
- *Obesity*
- *Arterial hypertension*
- *Previous pelvic radiotherapy*
- *Long-term tamoxifen*

The benefits of adjuvant treatment with tamoxifen outweigh the risks of recurrence. Although some hormone therapies with no endometrial interference are now available and have proven effective as adjuvant treatments (i.e. anastrozole), their cost is many times superior to that of tamoxifen, so their massive use as adjuvant treatments is not justified. Patients on tamoxifen should have pelvic and transvaginal ultrasound to evaluate the endometrial thickness at least once a year (it should not be bigger than 5-7mm). The same goes for women who present with abnormal vaginal bleeding.

Diagnosis

Endometrial biopsy through fractionated D&C.
CA-125 can be useful as tumor marker.

Treatment Options

- *Surgery: Abdominal hysterectomy with adenectomy, bilateral iliac lymphatic sampling and peritoneal enema cytology.*
- *Early stages: Adjuvant treatment with medroxiprogesterone in patients with high risk of relapse.*
- *Radiotherapy to avoid local relapse.*
- *Advanced stages:*
  - *Chemotherapy: standard drugs are cisplatin, doxorubicin and paclitaxel.*
  - *Radiotherapy.*
  - *Hormone therapy: medroxiprogesterone and tomoxifen.*

BREAST CANCER

Its incidence is substantially increasing. Breast cancer is the second leading cause of cancer death in the USA. The lifetime risk of women getting breast cancer is about 1 in 8 (12 %) (18). The natural history of this disease is characterized by long-term duration and heterogeneity amongst patients.

Risk Factors:

- *Family history: 5/10% of the cases, related to BCRA 1-1 genes*
- *Nuliparity*
- *Early menarche*
- *Advanced age*
- *Previous history of breast cancer*
- *Late menopausal age*
- *First pregnancy after 30 years of age*
- *Hormone replacement therapy*

Prevention:

- *Breast self examinations*
- *Breast palpation by gynecologist at least once annually*
- *Mammogram starting at age 45. A drop in breast cancer mortality was reported in 35% of patients between 50-69 years of age (19).*

Prognosis Factors:

- *Tumor size, type and histological level. Spreading stage*
- *Lymph nodes involvement*
- *Levels of estrogen and progesterone receptors in biopsy*
- *Menopausal condition*

Treatment Options:

- *Should be decided according to staging and prognosis*
- *Surgery: mastectomy and quadranectomy*
- *Radiotherapy: to avoid local recurrences and for bone metastasis (palliative)*
- *Hormone therapy: in patients with positive hormone receptors, radiotherapy may be offered as adjuvant (tomoxifen for 5 years) or as procedure of choice: for hormone-sensitive metastatic patterns (spreading to skin, bones, lymph nodes or pleuras). Tomoxifen is used as first line treatment; aromatase-inhibitors are effective as second line treatments (anastrozole, exemestane, letrozole). Premenopausal patients may be candidates for complete hormone blockade with LHRH analogues plus aromatase inhibitor. Oopherectomy may also be recommended.*
- *Chemotherapy: Standard drugs are: adriblastine, cyclophosphamide, fluorouracil, 5-FU, taxanes, vinorelbine, methotrexate, cisplatin, capecitalbine and trastuzumab. These drugs are habitually used in combined patterns, depending on disease stage (adjuvant or therapeutic) and on the drugs used in previous patterns. An analysis of cost-effectiveness of the procedure of choice is also to be considered.*

LUNG CANCER

Lung cancer is the most common cause of cancer death almost worldwide. In many countries, lung cancer overtakes breast cancer mortality amongst women.

Tobacco and Lung Cancer

Tobacco consumption is nowadays one of the greatest threats to human health. It is estimated that 1,100 million people smoke worldwide; 300 million living in industrialized nations and 800 million in developing countries. In industrial countries, tobacco consumption rate has dropped 1% in recent years, whilst consumption in developing countries has increased 1% per year. In 2000, seventy one percent of tobacco world production was consumed in developing countries (6).

Trading restrictions imposed on tobacco companies in industrialized nations have been particularly prejudicial for economically poor countries. To compensate for such loss, many corporations have settled in regions of the world where knowledge of tobacco-related diseases is scarce, which leads to alarming figures: in Venezuela, 40.5 % of the population smokes; cigarette consumption in Argentina has increased 9% in the last 10 years amongst women under 20; in Kenya, 40% of young people smoke tobacco and in China the incidence of lung cancer has increased 475% in the last years (3).

The risk of developing lung cancer in smokers is proportional to the number of cigarettes they smoke and to the power of four of the habit duration (years from the moment of taking up smoking). After quitting, the relative risk declines nearly 50 % after 5 years and 80% after 10 years.

Diagnosis

Although patients may sometimes be diagnosed through an incidental finding of an asymptomatic node in a thorax X-ray, most of the lung tumors are diagnosed through the emergence or worsening of clinical signs or symptoms. These can be classified into four categories:

1. Those induced by local or intrathoracic growth
2. Those related to distant metastasis
3. Non-specific symptoms
4. Paraneoplastic syndromes

Nearly 60 % of small cell lung cancers (SCLC) and 40% of non small cell lung cancers are diagnosed in late stages, and though virtually any organ might be a site of metastasis, the most frequent sites of hematogenous spread are the central nervous system (CNS), bones, liver and suprarenal glands. Bone pain occurs in 30 to 50% of the patients with bone metastases (6). An affected liver can develop with pain in the right hypochondria or non-specific symptoms such as nausea, vomiting, loss of weight or anemia. Most adrenal metastases are diagnosed accidentally during staging or during autopsies. The most frequent symptoms affecting the NCS are headaches, altered mental status, convulsions and focal muscle weakening.

Treatment Options

Treatment options for lung cancer depend on many factors, mainly the tumor biology and stage, the patient's health and the financial means available in the place where the disease is diagnosed.

In general terms, we should recommend the guidelines for lung cancer management provided by the National Cancer Institute (NCI) of the United States in its Physician Data Query (PDQ) (20) page for health professionals; however, these can rarely be applied to all people in the developing world.

For patients in stages I and II surgery is often the treatment of choice, while radiotherapy can be recommended for patients for whom surgery is clinically contraindicated. These treatment options can also be offered to patients with resectable stages III A NO-N1.

For patients with mediastinal nodular disease (N2) with no evidence of distant metastasis, treatment options include:

1 *Neoadjuvant chemotherapy with 2 or three cycles followed by surgery with survival 2 to 5 years superior to surgery alone.*
2 *Combined chemotherapy + radiotherapy, mainly when surgery alone is not a choice for treatment. (The combination of chemotherapy and radiotherapy highly increases complications during surgical procedures.)*

For unresectable stages IIIA or stages IIIB neoadjuvant chemotherapy can be offered during one or two cycles followed by thoracic radiotherapy, doses of approximately 60 Gy, over five weeks. A reasonable and inexpensive option is the combination of cisplatin and vinorelbine.

Another effective combination is cisplatin and etoposide (like paclitaxel and cisplatin, and four times less expensive), with responses of 12 to 27 %, in a 4.3 month progression.

Benefits of chemotherapy treatment are evident in patients in good health (performance status 0-1). In this group of patients, combinations based on cisplatin prolong survival and have considerable palliative effects. Many randomized trials comparing chemotherapy and the best supportive treatments showed not only advantages in the survival rates but also in the quality of life in patients who had been treated with chemotherapy. These benefits were not so clear in patients in poor health.

As regards optimum duration of these treatments, recent trials have shown that 3 or 4 cycles can be enough. Long-term treatments do not seem to improve survival and imply the risk of accumulative toxicity which conspires against the patients' quality of life.

SMALL CELL LUNG CANCER (SCLC)

Patients with disease confined to thorax (40 % of the cases) are mainly treated with two options within chemotherapy (20). The most frequently used combination worldwide is cisplatin and etoposide. A total of 4 cycles is recommended, and patients should be examined every two treatment cycles.

Another alternative is the combination of cyclophosphamide, doxorubicin and vincristine, but this regimen has a major drawback: it cannot be used simultaneously with radiotherapy, and thus it is generally used as a second line treatment. In patients with limited stage disease, thoracic radiotherapy should be offered simultaneously (only with the etoposide-cisplatin regimen) or sequentially, after radiotherapy has been completed.

In patients with extended stage disease (60 % of the cases), treatment combinations are the same as in the limited stage disease, only that in the former thoracic radiotherapy does not seem very useful. Management of Respiratory Symptoms:

Table 3 summarizes the most common clinical manifestations of lung cancer caused by local growth.

Table 3 – Clinical Manifestations of Lung Cancer Caused by Local Growth (21) Frequency (%)

Clinical manifestation	SCLC	NSCLC
Cough	50-76	40
Dyspnea	34-40	30-40
Chest pain	35-36	25-40
Hemopthysis	15-23	15-35
Pneumonitis	21-25	13-24
Vocal cord paralysis	15	infrequent
VCS Syndrome	12	5-7
Pleural hemorrhage	10-15	15
Pancoast Syndrome	rare	3
Pericardial hemorrhage	of low frequency	rare

The main are:
Dyspnea: Dyspnea is a symptom frequently associated to lung cancer, occurring in 30 to 40 % of the patients in the moment they are diagnosed, and even in 90 % in the late stages of the disease (21).

Lung tumors can cause dyspnea by direct effect, pleural hemorrhage, vena cava syndrome, carcinomatous lymphagitis, atelectasis, tracheal obstruction or tracheo-esophageal fistulae. Additionally other factors that can result in dyspnea or aggravate it are: heart failure, pericardial hemorrhage, chronic obstructive lung disease, infections, lung thromboembolism, anemia, cachexia, metabolic acidosis and anxiety.

As with other symptoms, dyspnea should be examined on a regular basis in order to know its intensity, its evolution and response to treatment. The most frequently used systems are Edmonton Symptom Assessment System (ESAS) and Support Team Assessment Schedule (STASS).

The optimum treatment for dyspnea is aimed at managing its reversible causes. When this is not possible, pharmacological and non-pharmacological methods are used to alleviate symptoms. Symptomatic treatment for dyspnea is based in three main elements: oxygen therapy, use of drugs and standard supportive treatments. Oxygen therapy is mainly recommended for hypoxemic patients. It can be continually supplied in patients with chronic obstructive lung disease or with lymphangitis (22). In cases of dyspnea associated to movements or exercise oxygen can be supplied intermittently. Oxygen supply is traditionally made through masks, but nasal cannulae are more comfortable.

Clinical benefits of the use of opioids in symptomatic treatment for dyspnea have been demonstrated by many clinical trials. The initial recommended dose is 5 mgs every four hours. If the patient is already taking opioids for pain treatment, doses should be increased 25 % if dyspnea is minor, and up to 50 % if it is moderate or severe (22).

There have been no clinical trials to assess benzodiazepines use in symptom management; however, they could be used in cases of anxiety or panic crisis. Steroids can be recommended for lymphangitis, bronchospasm and superior vena cava syndrome. Chronic use, however, may affect breathing mechanics as it functionally alters many muscle groups, mainly diaphragm.

Accumulated breathing secretions in the last days of patients with sensory depression may be treated with anticholinergics as intermittently supplied hyoscine or by continuous infusion.

Cough: Cough is a frequent symptom occurring in patients with lung cancer. Between 40 and 50% of patients have it at the moment of diagnosis and nearly 85% develop it at some point during the evolution of the disease.

Local anesthetics used in inhalations can be effective to relieve cough caused by endobronchial neoplasms. The most frequently used anesthetics are lidocaine 2% (5ml) and bupivacaine 0.25% (5ml) three or four times a day. As these agents inhibit deglutition reflexes, inhalations should not be done before or after food or drink intake.

Hemopthysis: Hemopthysis occurs in up to 35 % of patients with lung neoplasms (13). It is an extremely alarming symptom both for patients and relatives and leads to rapid consultation. It is generally determined by the tumor itself, though some associated causes may be bronchitis, pneumonia or thromboembolism.

External radiotherapy is highly effective and can palliate the symptoms in 90 % of the cases. Endobronchial radiotherapy and laser are also treatment options if the patient's general state allows for them.

In palliative care, massive hemopthysis can be considered real urgencies, but procedures such as intubations, bronchoscope and embolization of bronchial arteries are not recommended. In this case, the use of strong opioids and midazolam or diazepam may be recommended to reduce the sensation of fear and anxiety.

PROSTATE CANCER

Prostate Cancer is one of the most frequent neoplasms affecting men in developed countries. Although it is not very common in Asia, Africa and South America, its incidence rate is growing parallel to an increase in life expectancy.

Early detection through PSA tests together with digital rectal exams starting from the age of 50 in men with a life expectancy of at least 10 years can help diagnose a high rate of patients on an early stage potentially curable with surgery or radiotherapy.

At advanced stages, the disease generally develops with bone metastases producing low back pain radiated to pelvis and thighs. Antiandrogens hormonal therapy (flutamide alone or together with surgical or chemical castration) and Luteinizing Hormone Releasing Hormone (LHRH) agonists therapy often produce a response with partial remission of the disease and considerable pain palliation, in some cases over periods of years.

Watchful waiting can be appropriate particularly in elderly men with asymptomatic tumors. LHRH agonists' therapy is quite expensive and therefore should be considered as a second hormonal line, after flutamide progression. If hormonal therapy cannot be carried out, surgical castration may be an option as it produces the same hormonal response.

Palliative radiotherapy to sites of bone metastases with persistent or incidental pain is an excellent palliative oncological treatment. Hypofractionation techniques and a few radiotherapy sessions should also be considered.

MALIGNANT MELANOMA

A melanoma is a malignant tumor affecting melanocytes (cells derived from the neural crest). The majority of melanomas develop in the skin, but they can also be found in mucus, uvea, choroids and iris.

Up to 60% of melanomas could develop *de novo*, with no previous lesions, and 1-2% are amelanotic

(6). Malignant melanomas develop mainly in adults. From a practical point of view, any pigmented lesion changing in size, color (darkening or irregular color) or shape (uneven border) should be considered a melanoma.

In most of the cases diagnosis involves an excisional biopsy. This is an elliptical incision that removes the lesion and the layers of subcutaneous tissue beneath it, with a margin of at least 2mm of normal skin surrounding the lesion when the lesion is smaller than 1.5 cm.

Like in most of malignant diseases, causes of melanoma are regarded as multi factorial. However, many studies have related Ultra Violet (UV) radiation to genotypical, phenotypical and immunocompetence features in the genesis of the disease.

The melanoma morbidity and mortality rates have increased worldwide. Melanoma mortality has doubled in the last 35 years. The increase of recreational exposure to the sun, an increased UV radiation reaching the Earth and late diagnosis of the tumor are key factors related to this rising incidence.

The system used for staging melanoma is that of the AJCC's (23), which includes Breslowww and Clark's micro staging systems:

Breslow's micro staging system (tumor thickness)
I - Less than 0.75 mm
II - 0.76 to 1.5 mm
III - 1.51 to 3.99 mm
IV - 4mm or more
Clark's micro staging system (level of invasion)
I - Epidermis-limited melanoma
II - Invasive melanoma with superficial infiltration of the papillary dermis
III - Spreading to vessel plexuses of the papillary dermis
IV - Spreading to reticular dermis
V - Subcutaneous tissue compromised.

Key prognosis variables for the localized disease (stages I and II, AJCC) are the thickness of the lesion (Breslow), depth of invasion (Clark), ulceration and anatomic localization.

For advanced stages (III, AJCC), the number of regional nodes compromised is directly related to survival. In patients with metastatic melanoma (IV, AJCC) localization and number of metastases are key factors in prognosis.

There are no differences in diagnosis and therapy approaches in the most frequent growth patterns of melanoma (superficial melanoma, nodular melanoma, maligno lentigo melanoma and acral lentiginous melanoma). In all the cases an annual follow-up skin examination is recommended, as a as a ten-year disease-free survival cannot be considered a cure and the possibility of developing a second primary melanoma reaches 10%.

Standard Treatment Options

Local surgery (with the appropriate margins according to the lesion), diagnosis and treatment of the regional nodes affected, adjuvant treatment or the limitedly effective treatment of distant metastasis are today's treatment options depending on different levels evidence.

As regards lesion radial margins recommended for local surgical procedure, 1 cm is enough for lesions smaller than 1mm, and 2 cm are enough for lesions up to 4 mm.

As the possibility of regional metastatic spreading (lymph nodes) or distant metastasis increases, a sentinel node biopsy previous to any surgery should be considered.

In case a sentinel node is macroscopically or microscopically affected (false negatives 0 to 2%), surgery will include lymph node dissection. Moreover, patients with Breslow IV should be considered for adjuvant treatment.

Stage IV Treatment

Dacarbazine (DTIC) is the most active agent in metastatic melanoma treatment. Response (generally of not more than 6 months) is observed in nearly 20% of the patients (6). The most frequent toxicity is gastrointestinal and can be well controlled.

Although multiple poly chemotherapy, immunotherapy and bio chemotherapy regimens have been tested, there is no evidence to support the use of more complex treatments than DTIC, especially in developing countries.

Treatment of Recurrences

Like in the metastatic disease, decision on the treatment of recurrences depends on many factors (site of recurrence, previous treatments, available options, the patient's decision, etc.). Whenever possible, surgery is the most effective treatment (single localizations). Palliative radiotherapy can help relieve the symptoms of some sites (central nervous system, bone-marrow compression, bone metastasis pains). Hyperthermic perfusion in limb-localized recurrences is a complex procedure not widely available in developing countries.

CONCLUSION

As far as treatments for cancer are concerned, developing countries are totally heterogeneous in their approach. There are certain areas where diagnosis and treatment are proficient, whilst in others patients may find themselves totally unprotected. These differences can even exist within the same country.

The aim of this chapter is to promote effective early diagnosis methods, low cost effective treatments and palliative care. For the great majority of the advanced solid tumors, palliative care is, in many cases, the best option.

Although patients under more complicated treatments should be referred to first level oncological centers, the simplest standard treatments might be conducted in most of the sanitary centers,

possibly under specialized supervision through phone or Internet consultations.
Likewise, oncological centers in big cities should refer patients under palliative treatment to the places where they come from -even to rural areas- as long as adequate palliative care teams are made up to treat and take care of patients and their families in the best possible way.

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Recommended web pages:

Edmonton Program for Palliative Care, www.palliative.org

International Association for Hospice and Palliative Care www.hospicecare.com

International Union Against Cancer (UICC) www.uicc.org

World Health Organization cancer Control Program www.who.int/cancer/nccp/nccp/en/

7 Symptom Assessment in Cancer

Ahmed Elsayem, MD; Liliana De Lima, MHA

INTRODUCTION

Palliative care patients present multiple symptoms which are intense, long-lasting, multifactorial and constantly changing. One of the keys to develop appropriate strategies for symptom management is adequate and constant evaluation. This often requires the participation and collaboration of professionals from different disciplines developing strategies and therapeutic objectives based on the patients' needs.

The use of multi professional evaluation is complementarily to clinical observations. The structured use of evaluation tools aims at providing the greatest palliation possible of symptoms and allows for research and education in palliative care.

The cornerstone of appropriate, effective palliative care for patients with advanced cancer is through ongoing assessment. Moreover, because these patients present with multiple severe symptoms, it is clear that the best approach to evaluation and treatment is a multidisciplinary one. In recent years, it has become evident that appropriate assessment of a cancer patient with multiple symptoms requires a multidimensional evaluation of the symptoms and syndromes, the patient's clinical and psychosocial characteristics, and a number of specific prognostic factors that have a major impact on the treatment outcome might help focus the care.

Assessment in Special Populations

Assessment of symptoms can be challenging in many sub populations, including pediatric, cognitively impaired and illiterate patients.

Most of the assessment tools designed for the pediatric population portray "faces" scales with different levels of distress in the expression and observational scales. Some of these include the McGrath Scale, the Bieri Faces Pain scale, the Oucher Scale and the Olivares-Duran Pain scales for pain assessment. Observational scales used in children include the Children's Hospital of Eastern Ontario Pain Scale (CHEOPS) for children 1 to 7 years old (See chapter 14 of this publication).

Health care professionals working in developing countries and with illiterate populations, may have difficulty using the common Visual Analogue Scale (VAS) and Numerical Rating Scales (NRS). There have been some efforts to use figures and drawings as opposed to numbers in VAS to represent the absence or presence of symptoms. These include the Escala Frutal Analoga (EFA) developed in Mexico and the Visual Symptom Scale (VSS) developed in Colombia. The EFA uses fruits of different sizes to represent the heaviness and weight of pain (it hurts like a lemon or like a watermelon). The VSS uses faces and drawings of individuals to represent different symptoms (nausea, fatigue, vomit, diarrhea, constipation, etc) (See Addendum 1). Although these scales have not been validated, they may be useful in patients with limited or little literacy levels who have difficulty understanding the value of numbers and associating them to a subjective feeling.

Only very few instruments have proven to be culturally sensitive and thus valid and reliable across different cultural settings. One of the few which has been validated cross culturally is the Brief Pain Inventory (BPI), in both its long and short versions. Face scales are probably the most cross sectional validated tools and should be used not only in pediatric populations but also in illiterate patients, and in patients who speak a different language from that of the health care provider.

The use of assessment tools often faces methodological objections, including:

- *Lack of validation of a tool when translated from one language to another*
- *Lack of understanding (patient's illiteracy level)*
- *Cultural, social and ethnical aspects which can make certain tools inappropriate for some population groups*
- *Lack of clear guidelines stating how often a certain evaluation should be repeated*

In spite of all these restraints, however, there are tools which can have great clinical use in the patient with advanced cancer, whether in their original version or adapted to the target population in which they will be used.

ASSESSMENT PROCESS

Patients with pain and cancer require careful assessment to determine the nature of their complaints and begin appropriate treatment (Table 1). Careful evaluation should be paid to the characteristics of the symptoms as well as a detailed neurological examination.

The goal of the health care provider in evaluating and treating the manifestations of cancer is a dual one. The first and often understated goal is diagnostic: appropriately identifying the source of the problem. To accomplish this, knowledge of the natural history of the illness as well as appreciation of common symptoms occurring in disease and condition are essential. The second goal is therapeutic: to relieve or minimize the symptom using appropriate management techniques, thereby improving the patient's quality of life as best as possible..

Table 1	
1.	Cause (cancer, cancer treatment, not related to cancer)
2.	Intensity (visual analogue scale, numerical, verbal, etc.)
3.	Alcoholism/drugs (CAGE questionnaire, etc.)
4.	Psychosocial distress (somatization)
5.	Cognitive function (MMSE, etc.)
6.	Mechanism (neuropathic, nonneuropathic)
7.	Nature (continuous, incidental)
8.	Other related symptoms (ESAS, etc.)

MMSE: mini mental state questionnaire

ESAS: Edmonton Symptom Assessment System

CAGE questionnaire: 'CAGE' is a mnemonic for attempts to cut back on drinking, being annoyed at criticisms about drinking, feeling guilty about drinking, and using alcohol as an eye opener.

It is crucial to measure and monitor the intensity of the symptoms. This can be done simply using visual analogue scales, verbal scales, numerical scales, or more complex tools. Most of these instruments and techniques are very reliable in assessment of the intensity of symptoms. This assessment can be made more effective with a graphic display of the symptoms in the patient's chart along with that of other vital signs measured during the monitoring examination. This forms a basis for outcomes and helps to effectively administer appropriate care.

PSYCHOSOCIAL ASSESSMENT

Symptom assessment is not valid unless a thorough psychosocial assessment is done. The clinician should ask questions about psychological factors such as loss of independence, family problems, financial difficulties, social isolation, and fear of death. Often, cancer patients meet diagnostic criteria for the psychiatric diagnosis of adjustment disorder with anxiety and/or depressed mood.

In the past, simplistic, unidimensional assessment tools led to an overemphasis on pharmacological as well as interventional treatments. This simplistic approach may result in rapid escalation of opioid medication doses with the potential for opioid toxicity and other side effects as well as unsatisfied patients and family members.

The following are the poor prognostic factors for the management of cancer pain. A thorough assessment should be performed in patients who have them.

- *A positive history of alcoholism and drug abuse*
- *A history of pointing somatization as a result of affective disorders such as anxiety or depression*
- *Cognitive failure in patients with advanced cancer*
- *Mechanism of pain: neuropathic pain tends to be more refractory to treatment than*
- *nociceptive pain.*

The essential components of the initial assessment are:

- *Detailed history and physical examination*
- *Psychosocial evaluation*
- *Diagnostic imaging and laboratory studies as indicated.*

Continued treatment requires repeat assessment:

- *At regular intervals*
- *Whenever pain changes or new pain appears*
- *Whenever therapy changes.*

ASSESSMENT TOOLS

The tools described below, serve clinical, research, and educational functions by providing uniform, valid measures of symptom severity and allowing the clear communication of findings between patient and clinician and even between clinicians. In the process, these tools can lead to improved delivery of evidence-based, scientific care.

The Anderson Symptom Assessment System (ASAS)

The ASAS (see Table 2) is used to quantitatively evaluate the patient's perception of 10 symptoms: pain, fatigue, nausea, depression, anxiety, drowsiness, shortness of breath, appetite, sleep, and feeling of well-being. Each of these symptoms is rated by the patient on a scale of 0 -10 (where 0 equals no distress and 10 equals the worst imaginable distress related to that symptom). Note that a score of 0 for pain, fatigue, nausea, depression, anxiety, drowsiness, and shortness of breath indicates the absence of these symptoms; conversely, a score of 0 for appetite, sleep, and feeling of well-being represents the best-case scenario in these areas. Either patients or their caregivers can complete the form.

The ASAS form is completed at each visit for outpatients and as often as daily for inpatients. When the numerical ratings are summarized graphically, rapid analysis of the patient's overall perception of suffering is possible. Moreover, when symptoms are assessed daily, this graphic representation enables clinicians to easily see trends in symptom control as they develop. The interpretation of these graphic trends can then lead to better clinical decision making that is determined by a preponderance of one or several symptoms in the entire constellation of symptoms. Certain symptom patterns may emerge depending on the patient's actual physical expression of symptoms, as opposed to somatization, or upon the patient's coping skills.

TABLE 2: ANDERSON SYMPTOM ASSESSMENT SYSTEM

Patient Name_____

Date:_____

No Pain	0	1	2	3	4	5	6	7	8	9	10	Worst Pain Imaginable
No Fatigue	0	1	2	3	4	5	6	7	8	9	10	Worst Fatigue Imaginable
No Nausea	0	1	2	3	4	5	6	7	8	9	10	Worst Nausea Imaginable
No Depression	0	1	2	3	4	5	6	7	8	9	10	Worst Depression Imaginable
No Anxiety	0	1	2	3	4	5	6	7	8	9	10	Worst Anxiety Imaginable
No Drowsiness	0	1	2	3	4	5	6	7	8	9	10	Worst Drowsiness Imaginable
No Shortness of Breath	0	1	2	3	4	5	6	7	8	9	10	Worst Shortness of Breath Imaginable
Best Appetite	0	1	2	3	4	5	6	7	8	9	10	Worst Appetite Imaginable
Best Sleep	0	1	2	3	4	5	6	7	8	9	10	Worst Sleep Imaginable
Best Feeling of Wellbeing	0	1	2	3	4	5	6	7	8	9	10	Worst Feeling of Wellbeing Imaginable

Assessed by:_____

The CAGE Questionnaire

The CAGE (See Table 3) questionnaire is a screening tool for alcoholism that may reveal a patient's poor coping mechanisms and especially the possibility of a patient using chemical means to cope with stress. A patient with dysfunctional coping skills may present a challenge to the satisfactory management of problematic symptoms, especially pain. The CAGE questionnaire queries the patient about his or her self-perception and others' comments regarding the patient's drinking. The questions refer to lifetime experience and not to any specific or limited time frames in the patient's history. A simple series of four questions is asked: two or more positive responses is considered an indication of dysfunctional coping skills. To improve the validity of the CAGE results, the questionnaire should be completed as part of the initial assessment and especially prior to asking the patient about amounts of alcohol or drugs ingested.

TABLE 3: THE CAGE QUESTIONNAIRE

Patient Name_____

Date:_____

Have you ever felt that you should cut down on your drinking of alcoholic beverages? * do not continue if patient has NEVER had a drink*	Yes	No
Have you ever been annoyed by people criticizing your drinking of alcohol?	Yes	No
Have you ever felt bad or guilty about your drinking?	Yes	No
Have you ever had a drink first thing in the morning or a drink to get rid of a hangover (eye-opener)?	Yes	No

Comments: _____

_____

_____

Assessed by _____

Mini Mental State Assessment (MMSE)

The MMSE (see Table 4) is a valid, widely used screening tool for evaluation of cognitive function. The MMSE assesses a patient's orientation to time and place, immediate recall, short-term memory, language, and ability to understand and perform simple construction tasks. The test is simple to administer and requires only a short time to complete. The unadjusted maximum score is 30. An adjusted score, which considers age and education level and is calculated using a chart included in the MMSE, should be used as the maximum for an individual patient. A score of ≥ 24 is considered normal; a score of ≤ 23 generally indicates cognitive impairment. In the presence of cognitive impairment the numerical assessment of symptoms may not be valid and clinicians may refer to prior assessment or other cues to manage symptoms.

Functional Independence Measure

The functional status of patients with advanced cancer can be assessed using the Functional Independence Measure (FIM) (See Table 5). On a scale of 1- 7, the 15-item FIM measures the patient's total dependence versus independence in several functional areas (i.e., eating, grooming, upper and lower extremity dressing, toileting, transfers, ambulation, comprehension, expression, social interaction, problem solving, and memory). For each area, a score of 1 equals total dependence, and a score of 7 equals independence. The highest possible total score on the FIM is 105. When trends in the functional measures are followed over time, the patient's functional performance can be assessed throughout the progression of disease and symptom burden. At M. D. Anderson, a FIM is included in the Interdisciplinary Assessment and Plan of Care form.

TABLE 4: MINI MENTAL STATE ASSESSMENT ©1975, 1998 Mini Mental LLC

Patient Name_____

Date:_____

Maximum Score	Patient Score	Question
5		1. What is the (day) (month) (year) (season)?
5		2. Where are we? (city?) (state) (country) (hospital) (floor)?
3		3. state 3 objects and ask patient to remember them (i.e.: Glass, blanket, pencil)
5		4. Spell WORLD backwards (DLROW)
3		5. Ask the patient to name the 3 objects above. If unable to name, give patients cues but score only for objects named without cues
2		6. Ask patient to name these objects: Pen, Watch (or 2 other objects in the room)
1		7. Ask the patient to repeat the following: "No ifs, ands or buts"
3		8. Have patient follow three stage command: "Take this sheet of paper in your right hand, fold it in half, and give it back to me"
1		9. Read and obey the following: CLOSE YOUR EYES
1		10. Write a sentence (give the patient a topic)
1		11. Copy the design in next page (or another)
30		TOTAL SCORE

** Please make a note of any delay/hesitancy to respond or omissions. If score =0, specify reason

AVERAGE SCORES

Compare the patient's scores with the average

Years of Schooling	**Age**					
	<40	40-49	50-59	60-69	70-79	>79
0-4	20	20	20	19	18	16
5-8	24	24	25	24	23	22
9-12	28	28	27	27	26	23
College or higher	29	29	28	28	27	26

TABLE 5 – FUNCTIONAL INDEPENDENCE MEASURE

	Independence ←						→ Total Dependence
	1	2	3	4	5	6	7
Eating							
Grooming							
Upper Extremity Dressing							
Lowe Extremity Dressing							
Toileting							
Transfer - Bed/WC							
Transfer – Toilet							
Transfer – Tub							
Walk – WC							
Stairs							
Comprehension							
Expression							
Social Interaction							
Problem Solving							
Memory							
Total Performance							

In summary a thorough multi-dimensional pain assessment is key to successful management of pain and other symptoms in cancer patients.

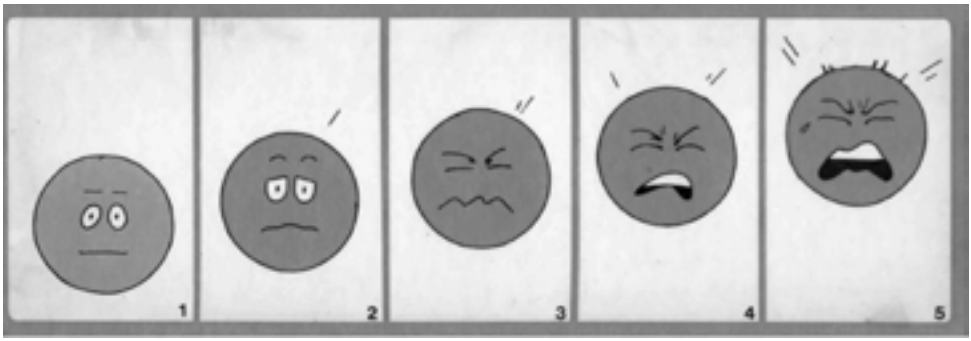
Palliative Pearls

- *Proper assessment is vital for good symptom management.*
- *A multidimensional approach is essential for symptom control in patients with advanced cancer.*
- *Be aware of poor prognostic factors in pain and symptom management.*
- *Cognitive failure prevents accurate assessment of symptoms and should be corrected if possible.*
- *Psychological distress has a significant impact on symptom expression.*
- *The CAGE questionnaire is a measure of coping chemically with stresses, which may put the patient at risk of abusing opioid medications. The current use of alcohol or the amount used is of less importance.*

* From: Mini Mental State: A Practice for Grading the Cognitive State of Patients for the Clinician. *Journal of Psychiatric Research* 12(3):189-198; 1975. for Clinical use of the MMSE, permission must be obtained from Mini Mental LLC – 31st St. James Ave., Suite 1, boston, MA 02116, USA.

CHAPTER 7 – SYMPTOM ASSESSMENT IN CANCER
ADDENDUM 1 – VISUAL SYMPTOM SCALE (VSS) FOR ILLITERATE PATIENTS*

PAIN INTENSITY



To the Patient: "Which one of these figures represents the intensity of the pain you are feeling now?

SOMNOLENCE



To the Patient: "Which of these situations best represents your present condition?

VOMIT



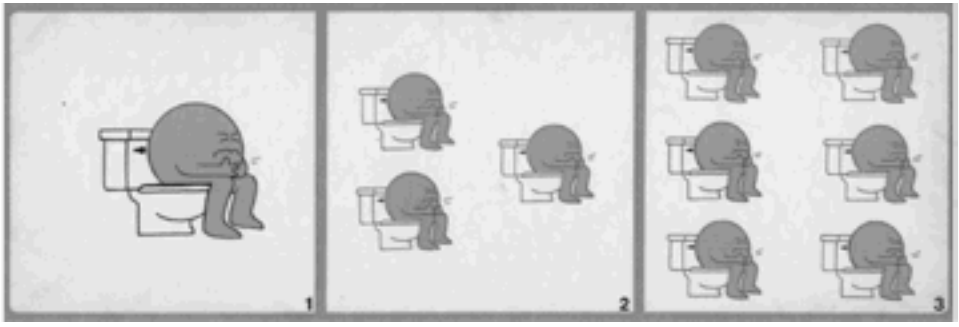
To the Patient: "Which of these situations best represents your present condition?"

INSOMNIA



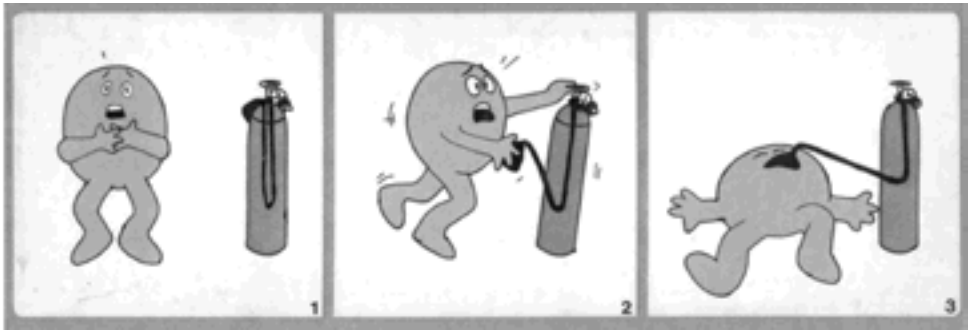
To the Patient: "Which of these situations best represents your present condition?"

DIARRHEA



To the Patient: "Which of these situations best represents your present condition?"

DYSPNEA



To the Patient: "Which of these situations best represents your present condition?"

CONSTIPATION



To the Patient: "Which of these situations best represents your present condition?"

* Note: The Visual Symptom Scale (VSS) was designed to help patient auto evaluation in a hospice program in Colombia, where the majority of the patients were illiterate. The scale was used for several years, and although it has not been scientifically validated, the editors feel it is important to include it in this publication to help aide individuals who are working with similar patients in developing countries. (Developed by Liliana De Lima (1992); Scientific advisor: Professor Eduardo Bruera; Illustrations: Jaime Troncoso)

Recommended Readings and Resources:

- Guevara U, Olivares E. La Medición del Dolor. In: Medicina del Dolor y Paliativa. Uriah Guevara Lopez and Ramon De Lille (eds) Corporativo Intermedica SA, 2002.
- Ingham J, Portenoy R. The Measurement of Pain and Other Symptoms. In: Oxford Textbook of Palliative Medicine (2nd Ed). Derek Doyle, Geoffrey Hanks and Neil MacDonald (eds). Oxford University Press, 1998.
- Dussel V. Valoración de Síntomas en Pacientes Pediátricos. In: Cuidados Paliativos: Guias para el Manejo Clínico (2nd Ed). Eduardo Bruera and Liliana De Lima (eds). Pan American Health Organization, 2004.
- Elsayem A, Driver L, Bruera E (eds). The MDACC Symptom Control and Palliative Care Handbook (2nd ed) UTMDACC, 2003.
- IAHPC Symptom and Research Tools webpage at http://www.hospicecare.com/resources/pain-research.htm

8 Cancer Pain

Sure h K. Reddy, M.D., F.F.A.R.C.S.

GENERAL PRINCIPLES

Pain tends to be one of the major symptoms in cancer patients, experienced during active treatment as well as in the advanced and terminal stages of cancer. Some cancer pain syndromes tend to be intractable secondary to the nature of the pain and attributable to co-morbid medical as well as psychological factors associated with serious illnesses, a terminal prognosis, and dying.

Definition of Pain

The International Association for the Study of Pain has defined pain as "an unpleasant sensory and emotional experience associated with actual or potential tissue injury or described in terms of such damage." The intensity of pain varies with the degree of injury, disease, or emotional impact. A second definition of pain might be "suffering or distress." Thus, pain is a self-reported subjective experience involving sensory neural transmission of the afferent noxious stimulation that has an expressive component manifesting the person's reaction to the painful stimulation. The definition of self-reported pain"Pain is whatever the experiencing person says it is, existing whenever he/she says it does" is an oversimplification that dismisses the influence of somatization and maladaptive coping mechanisms

Barriers to Pain Management

Despite the fact that up to 90% of cancer pain can be satisfactorily controlled using relatively simple medication regimens, we continue to under treat pain, and at least 25% of cancer patients die with pain. This discouraging fact is due to multiple reasons:

- *Inadequate assessment of pain*
- *Inadequate knowledge about pain and its treatment*
- *Concerns about possible side effects of pain medications*
- *Patients' and physicians' attitudes, fears, and misconceptions about pain and opioids*
- *Misinformation about opioid tolerance and dependence issues*
- *Poorly accessible or unavailable pain management services*
- *Improper and misguided regulation by governing agencies.*

These deficiencies are being addressed on multiple fronts to enhance pain management efforts. Because of the obvious need recognized by the medical establishment coupled with public demand for improved pain management, many hospitals are revising their curricula to improve education about pain assessment, treatment options (opioids and adjuvant analgesics), and side effects. Various groups such as the American Cancer Society, the International Narcotics Control board (INCB) and the World Health Organization (WHO) are working to improve cancer patient awareness about pain treatment. Local chapters as well as the WHO Center for Policy and Communications in Cancer Care in Wisconsin are working diligently to improve morphine availability in some countries.

Apart from these forward movements to bring down the barriers to adequate pain treatment; it is the simple moral obligation of every physician who treats cancer to become proficient in the basic assessment and management of pain and concomitant symptoms and side effects. In developing countries the barriers seems to be all of the above mentioned factors, but complex regulatory maze, as well as physicians attitude and lack of knowledge of opioid use in cancer pain seem to be the main barriers.

Impact of Pain

Severe pain in the patient with advanced cancer has negative physiological and psychological ramifications that may worsen an already bad situation. The interaction of pain with concurrent symptoms such as anorexia, nausea, constipation, delirium, dyspnea, depression, anxiety, and insomnia may compound the entire constellation of problems. The patient's functional status is further impaired, autonomy is compromised, and personal dignity is challenged. The patient and family may interpret progressive pain as a herald of impending death. They should be reassured that every effort will be made to bring pain and other symptoms under the best possible control.

Causes of Pain

Pain in the cancer patient may be due to one or several causes:

Tumor related

- *Tumor impingement on adjacent organs, tissues, nerves, bone, or vessels*
- *Inflammation due to tumor-induced mediators (e.g., interleukins, kinins, etc.)*

Treatment related

- *Postsurgical pain syndromes (e.g., following thoracotomy, mastectomy, amputation)*
- *Postchemotherapy pain (e.g., due to polyneuropathy, osseous necrosis, mucositis)*
- *Postradiation pain (e.g., due to neural fibrosis, myelopathy, osseous necrosis, mucositis)*

Noncancer Pain

- *Unrelated pain (e.g., myofascial, musculoskeletal)*
- *Nonphysical pain (e.g., spiritual pain, suffering)*

Most patients have at least one type of pain caused directly by the cancer, and most patients with advanced cancer have two or more types of pain. In general, about 60-65% of patients with advanced cancer will have pain due to direct tumor involvement, 20-25% will have treatment-related pain, and 10-15% will have pain unrelated to their cancer or its treatment.

Types of Pain

Pain may be described by its temporal course (acute or chronic) and pathophysiological mechanism and character (nociceptive or neuropathic). The patient with advanced cancer generally has chronic constant pain intermittently punctuated by acute breakthrough pain. Patients may have acute pain related to specific events such as surgery or other treatment. Some patients may have episodic pain that does not follow any pattern. Erratic intermittent pain may prove difficult to manage. The predominant mechanisms of cancer pain include nociceptive pain (both somatic and visceral) and neuropathic pain. Recent multinational data revealed that 72% of cancer patients have somatic nociceptive pain, 35% have visceral nociceptive pain, and 40% have neuropathic pain. Classifying pain enables us to better delineate its pathophysiology and facilitates treatment efficacy.

Nociceptive pain

- *Due to stimulation of nociceptors with afferent impulses propagated along the spinothalamic nociceptive pathways*

  Somatic (skin, bone, muscle, vessels, mucosa)
  - *Constant, waxing and waning, or intermittent*
  - *Gnawing, aching, occasionally cramping*
  - *Localized*

  Visceral (organs)
  - *Constant, waxing and waning*
  - *Aching, squeezing, cramping*
  - *Poorly localized, may possibly be referred.*

Neuropathic pain

- *Due to compression, invasion, destruction, or dysfunction of the CNS or peripheral nervous system (but the various pathophysiological mechanisms are poorly understood)*

  Protopathic or dysesthetic pain (e.g., deafferentation)
  - *Constant, waxing and waning*
  - *Burning*
  - *Localized but sometimes radiating (e.g., postherpetic neuralgia)*
  - *Epicritic or lancinating pain*
  - *Paroxysmal*
  - *Sharp, shooting (e.g., trigeminal neuralgia)*

CANCER PAIN MANAGEMENT

There are numerous approaches that can be used to manage cancer pain. In particular, the multiple modalities approach includes pharmacological, anesthetic, physical, behavioral/psychological, and neurosurgical methods.

Guidelines for Treatment of Cancer Pain

Various organizations have proposed guidelines for treating cancer pain, including the WHO with its simple and widely used three-step analgesic ladder (See Figure 1).



*WHO Ladder (Figure 1): In 1980's WHO proposed a three step analgesic ladder which involved a simple and effective way to manage cancer pain. It is a simple, well-validated, and effective method for rational titration of therapy for cancer pain. It relieves pain in approximately 90 percent of patients with and over 75 percent of cancer patients who are terminally ill. The five essential concepts in the WHO approach to drug therapy of cancer pain are: By mouth, By the clock, By the ladder, for the individual, with attention to detail. The initial step involves using non-opioid medications like acetaminophen, non-steroidal anti-inflammatories, with adjuvant medication if indicated, for mild pain. If pain persists, then opioids like codeine, hydrocodone may be added, while continuing non-opioids as well as adjuvant medications. If the pain persists and gets into severe stage, then stronger opioids like morphine, oxycodone, and hydromorphone may be added. Recent guidelines emphasize the need for flexibility and individualized assessment and treatment.

The Agency for Health Care Policy and Research (AHCPR) produced *Clinical Practice Guideline No. 9: Management of Cancer Pain* offers a comprehensive review of assessment and treatment principles. Others are offered by the American.

Pain Society, American Society of clinical Oncology (ASCO), and the American Society of Anesthesiologists.

The principles of pain treatment are guided by pain severity, previous opioid use, dosing, side effects, and pre-existing conditions.

Pain Severity

The pain severity guides in the process of choosing a low-potency opioid versus a high-potency drug like morphine. Most low-potency opioids are less suitable for high-grade pain due to dose limitations and presence of a ceiling effect. Most cancer pain situations require high-potency opioids. If a patient took part in an optimal trial with oral opioids, including rotation to different opioid, or experienced dose-limiting side effects, then an alternative route like the iv/sc and neuroaxial routes may be tried. Pain severity reported on a verbal numeric scale should be interpreted in the context of other psychosocial symptoms.

Opioid History and Side Effects

Patient-to-patient variability in the responses to a specific opioid has been widely appreciated and documented. Some patients' pain may respond surprisingly well to one opioid after failing or development of side effects to others, which is probably accounted for by the mechanism of action on different receptors as well as genetic factors in opiate receptor constitution. This phenomenon will obviously influence drug selection within the same class.

Previous Opioid Dosing And Pharmacokinetics

Previous opioid dosing and pharmacokinetics reflect the degree of tolerance to opioids, as opioid naïve patients will obviously require lower doses at least initially. Furthermore, opioid tolerant patients with constant pain are more likely to require around-the-clock, scheduled medications, while an "as needed" type regimen is recommended for patients with incident pain syndromes.

Pharmacotherapy

Pharmacotherapy remains the mainstay of cancer pain treatment. Most cancer pain syndromes present with moderate to severe pain associated with several co-morbid problems, necessitating the multidisciplinary approach for optimal treatment of them.

Pharmacotherapy consists of non-opioid and opioid medications based on the specific pain syndrome and other factors.

Nonopioid Drugs

- *NSAIDS*
- *Antidepressants*
- *Anticonvulsants*
- *Corticosteroids*
- *Phenothiazines*
- *Anesthetics*
- *Antiarrhythmics*
- *Benzodiazepines.*

Opioid drugs

- *Weak opioids*
- *Strong opioids.*

PRINCIPLES OF PHARMACOTHERAPY

- *Match the drug to the pain syndrome*
- *Have low threshold for prescribing opioids*
- *Add adjunct medications where appropriate*
- *The oral route should be the route of choice*
- *Use the iv route for acute titration*
- *Treat side effects before switching opioids*
- *Sequential opioid trials should be performed (two to three drugs)*
- *Be familiar with equianalgesic dosing*
- *Be familiar with the pharmacokinetics of opioids*
- *Differentiate between tolerance, physical dependence, and addiction.*

Opioids

- *Morphine is the drug of choice- for first-line treatment.*
- *Others drugs include oxycodone, hydromorphone, fentanyl, and methadone.*
- *Baseline and breakthrough combinations are commonly used.*
- *If a patient has only breakthrough pain, a short- acting opioid is preferred.-*
- *Oral transmucosal fentanyl may be the drug of choice for quick-onset and short duration pain.*
- *The oral route is preferred, but the iv and sc routes are used in certain situations.*

Weak opioids/Step 2 of WHO

- *Codeine*
- *Hydrocodone*
- *Propoxyphene*
- *Used for mild to moderate pain*
- *Not available as single agents*

- *Dose limited by the acetaminophen dose.*

Strong Opioids/Step 3 of WHO

- *Short half-life*
- *Morphine*
- *Hydromorphone*
- *Oxycodone*
- *Meperidine*
- *Fentanyl*
- *Oral transmucosal fentanyl citrate*
- *Sufentanyl*
- *Long half-life*
- *Methadone*
- *Levorphanol*
- *Transdermal fentanyl.*

Opioids: General Principles

Pure opioid agonists in single-agent form are preferred for treating cancer pain. These include morphine, hydromorphone, fentanyl, oxycodone, and methadone. Hydrocodone and codeine come mixed with acetaminophen, although the latter is also available as a single agent. There is no ceiling effect with opioids, and the dosage may be increased in small increments until the desired analgesic effect is achieved or side effects start to emerge. Pure opioid agonists usually have additive effects when used in combination.

Opioid Partial Agonists and Mixed Agonist-Antagonists

Opioid partial agonists (e.g., buprenorphine) and mixed agonist-antagonists (e.g., butorphanol, nalbuphine, and pentazocine) have limited or no use in treating cancer pain because of their mixed receptor activity, ceiling effect, side effects, and withdrawal problems.

Routes of Administration

- *The preferred route of opioid administration is oral, but other routes are acceptable if necessary because of dysphagia, delirium, obtundation, or bowel obstruction. These alternate routes include the following:*
- *Rectal: safe, inexpensive, and effective but inappropriate for patients with anorectal lesions or severe thrombocytopenia; most opioids are available in or can be compounded into suppository form; absorption may be variable*
- *Transdermal: convenient, but lengthy times required for titration; best used for stable pain syndromes. Difficult to titrate in acute painful situations. Available in many developing countries but at high cost.*
- *Transmucosal: The only preparation available is transmucosal fentanyl citrate. Ideal for breakthrough pain because of quicker absorption from the buccal mucosa. Not yet available in developing countries.*
- *Parenteral : equally effective are intravenous(iv) and subcutaneous routes (sc); regular intermittent*

sc administration likely as effective as continuous administration; equianalgesic dose conversion is easily calculated; used for acute titration or in situations where other routes are not feasible

- *Neuraxial: epidural or intrathecal opioids may be indicated in some situations, especially intractable situations involving neuropathic and combination pain syndromes.*

Starting Opioid Therapy

- *Begin with conservative around the clock (atc), dosing schedules every 3-4 hours with short acting opioid dosing schedules and provide adequate rescue dosing for breakthrough pain every 1-2 hours.*
- *Titrate the medication rapidly over 3 - 4 days to achieve pain relief and then convert to a maintenance regimen.*

Opioid Maintenance

- *Frequent assessment of the patient should include evaluation for the desired opioid effect, signs of side effects or toxicity, and evidence of disease progression.*
- *Upward titration of opioids will be necessary as tolerance develops or disease advances, both of which may yield increased pain.*
- *Downward titration may be indicated if:*
  - *Pain improves due to other palliative therapy (e.g., irradiation and after a nerve block)*
  - *Satisfactory pain control is accompanied by excess sedation*
  - *Toxicity appears.*

Adverse Effects of Opioids

- *Patients who require opioids in high doses or for a prolonged time or who develop renal insufficiency may accumulate toxic opioid metabolites and manifest signs of toxicity, including intractable nausea, somnolence, or pruritus. Signs of neurotoxicity include hallucinations, delirium, myoclonus, and hyperalgesia.*
- *Treatment measures include hydration and opioid rotation, which will usually obviate the need for benzodiazepines or other drugs used to treat myoclonus and addressing underlying metabolic factors. Symptomatic treatment may include haloperidol for delirium (see Chapter 7, Delirium).*
- *In patients with renal insufficiency, opioid doses should probably be reduced, even in the absence of overt signs of toxicity, because of the likely accumulation of metabolites. Methadone may be the drug of choice in such cases.*

Adjuvant Analgesics

Some medications originally developed to treat medical conditions other than cancer have been found to have pain-relieving qualities. These medications, called "adjuvants", help or assist main line drugs like opioids. The obvious examples are neuropathic pain syndromes such as postchemotherapy polyneuropathy, postherpetic neuralgia, and various regional neural plexopathies. Antidepressants, anticonvulsants, local anesthetics, anti-inflammatories, and antihypercalcemic agents may serve as adjuvant analgesics or mitigate the side effects of other drugs. However, because they are generally less reliable than opioids, treatment with such adjuvants should only be instituted after an optimal trial of primary opioid analgesics. Therapy with adjuvants should be initiated gradually to avoid likely side effects, even though this leads to a slower onset of effect. Consequently, it may take weeks to

noticeably reduce pain. The response of individual patients to adjuvants can vary substantially, and sequential titration trials may be needed to identify and optimize the best agent.

TABLE 1 – MAIN ADJUVANT ANALGESICS

Adjuvant Analgesics
- *Tricyclic antidepressants (amitryptiline, Nortriptyline)*

Anticonvulsants
- *Gabapentin*
- *Topiramate*
- *Leeitiracetam*
- *Tiagabine*
- *Oxcarbazepine*
- *Lamotrigine*
- *Felbamate*

Local Anesthetics
- *Lidocaine*

NMDA Receptor Antagonists
- *Ketamine*
- *Methadone*
- *Dextromethorphan*

Topical Analgesics
- *Capsaicin*

Miscellaneous drugs (psychotropic drugs, benzodiazepines, *bisphosphonates, steroids)*

Commonly employed adjuvants include the following

- *Amitriptyline/nortriptyline 10 - 25 mg hs titrated up to 150 mg hs for neuropathic pain*
- *Gabapentin 100 mg tid titrated up to 300 mg tid for neuropathic pain (up to 900 mg qid in severe cases). Sodium Valproic acid and clonazepam are commonly employed antiepileptic drugs for neuropathic pain in developing countries due to their low cost.*
- *Dexamethasone 10 mg po/iv/sc tid and then tapered to effect for neuropathic, bone, and visceral pain.*

Corticosteroids in Spinal Cord Compression

The ideal corticosteroids and their appropriate doses are controversial.

However, an uncontrolled trial found that administration of 100 mg of dexamethasone iv followed by 96 mg daily for 3 days concurrent with XRT and tapered over 2 weeks resulted in pain relief in 82% of patients

Bisphosphonates

- *Widely studied for the treatment of metastatic bone pain.*
- *Following systemic absorption, they localize to bone and inhibit osteoclast activity.*
- *Clodronate and pamidronate have been studied extensively in multiple myeloma and breast cancer.*
- *Zoledronic acid has also been approved recently to be used in the above situations.*

NSAIDs Cyclooxygenase-2 Inhibitors for Bone and Inflammatory Pain

- *Act by inhibiting COX enzyme peripherally*
- *Evidence suggests that they may have a central effect (McCormack, 1994).*

Non-Steroidal Antiflammatory Drugs (NSAIDs)

- *Exhibit a ceiling effect*
- *Do not exhibit tolerance and physical dependence*
- *Cause end organ toxicity*
- *Cox -2 inhibitors cause less GI and platelet dysfunction but other side effects are the same, e.g. celecoxib and rofecoxib, valdecoxib.*

COX2 Inhibitors

Recently there has been an explosion in the use of this class of drugs.

- *Celecoxib and Rofecoxib have gained popularity due to fewer gastric side-effects and minimal inhibition of platelets (ideal for the cancer population).*
- *A recent article (metaanalysis) raised the issue of a possible increased risk of cardiovascular events withCOX-2 inhibitors (Mukherjee et al, JAMA, 2002). Debate is ongoing.*

Practical Tips To Manage Cancer Pain Pharmacologically

The rational management of pain in a patient with advanced cancer depends on the patient's pain type, intensity, and previous exposure to opioids.

Opioid-Naïve Patient:

Initial evaluation:

- *Is the pain cancer-related? (Rule out nonmalignant causes.)*
- *What is the severity of the pain? (on a 0-10 scale)*
- *Where is the pain? (Consider the need for radiation or other therapy.)*
- *What is the baseline renal function? (Neurotoxic opioid metabolites may accumulate in the dehydrated or renal-insufficient patient.)*

Initiation and titration of analgesics

- *Acetaminophen 300 mg and codeine 30 mg (maximum 13 tablets/day) 1 - 2 tablets q4h as needed (prn).*
- *Acetaminophen 325 mg and hydrocodone 5 -10 mg (maximum 10 tablets/day) 1 - 2 tablets q4h prn (as needed).*
- *Remember to add an antiemetic and laxative to the regimen:*
  - *Antiemetic regimen: metoclopramide 10 mg q4h atc and 10 mg q2h prn for breakthrough nausea for 3 days followed by 10 mg q3h prn.*
  - *Laxative regimen: sennoside 8.6 mg 1 - 2 tablets bid and docusate 240 mg 1 - 2 qhs.*
- *Frequently assess for effect and side effects.*

If a stronger opioid is indicated initially or early in the course of treatment:

- *Morphine 10 mg po (5 mg iv/sc) q4h and 5 mg po q2h prn for breakthrough pain*
- *Hydromorphone 2 mg po (1 mg iv/sc) q4h atc and 1 mg po (0.5 mg iv/sc) q2h prn for breakthrough*

pain. Not available in many developing countries.
- *Oxycodone 5 mg po (iv/sc form not readily available) q4h atc and 5 mg po q2h prn for breakthrough pain. Not available in many developing countries.*
- *Continue antiemetic and laxative regimen*
- *Continue frequent assessment.*

Maintenance regimen
- *Continue current regimen as long as it is effective and needed.*
- *Add an adjuvant analgesic as indicated.*
- *If desired, change to a SR (sustained release) opioid.*
  - *Determine the total 24-hour opioid dose in mg (atc + prn doses).*
  - *Using an opioid conversion table, , convert to a daily equivalent dose of opioid-SR:*
  - *Morphine-SR, oxycodone-SR, or hydromorphone-SR q12h atc*

  or
  - *Transdermal fentanyl q72h.*
- *Treat breakthrough pain with a short acting opioid given q2h at 10-15% of the daily opioid-SR dose (e.g., for a patient on morphine-SR 100 mg q12h, give morphine-IR 20 mg q2h prn).*
- *We advise using the same opioid for both around the clock (atc) and breakthrough dosing, although using different drugs may be necessary in some situations.*
- *Continue antiemetic and laxative regimen, adjusting dosage as necessary.*
- *Continue adjuvants as indicated.*
- *Continue frequent assessment.*

Opioid-Tolerant Patient
- *Continue with ongoing evaluation of pain and treatment.*
- *Ascertain patient's response to previous opioids along with side effects.*

(Avoid opioids that have been ineffective or caused side effects.)
- *Determine total daily opioid dosage as above, increase by 30%, and give in divided doses q4h with q2h breakthrough dosing.*
- *Continue antiemetic and laxative regimen, adjusting as indicated.*
- *Continue adjuvants as needed.*
- *Continue frequent assessment.*
- *Increase opioid dosing as needed as described above.*
- *Convert to SR/IR regimen as described above.*
- *If toxicity or side effects become problematic, treat as indicated, and consider opioid adjustment or rotation to an alternative opioid.*

INTRACTABLE PAIN

If the patient's pain is refractory to progressive escalation of treatment, consider concurrent confounding problems:
- *Progression of the disease*
- *Psychological factors like anxiety, depression, and adjustment disorder as contributing factors*
- *Previous or ongoing problems with chemical dependency*
  - *Counsel the patient about the difference between nociception and suffering in pain*

expressions, and about the difference between analgesia and coping chemically.
  - *Consider restricting treatment to long-acting opioids with limited extra doses. Opioids should be prescribed for these patients by one physician only.*
  - *Assess the patient using the CAGE questionnaire (see Chapter 7) for alcoholism. Positivity may indicate patient's tendency to cope stress with chemicals, which includes opioid medications. CAGE positivity may help with damage control, if patient is showing signs of opioid toxicity.*
- *Depression or anxiety*
  - *Assess and treat the patient as outlined in Chapter10.*
  - *Consider psychiatric consultation.*
- *Somatization of chronic pain*
  - *Discuss with the patient the difference between pain caused by noxious stimuli and the pain of chronic suffering.*
- *Breakthrough pain*
  - *Escalate the opioid prn dosage and add methylphenidate 5 mg in the morning and 5 mg at noon if drowsiness or sedation becomes a problem.*
  - *Consider radiation therapy or surgical consultation if indicated.*
- *Bone pain*
  - *Consider NSAIDs (preferably COX-2 inhibitors).*
  - *Consider bisphosphonates (e.g., pamidronate 90 mg iv q 4 wk) or Zoledronic acid 4 mg IV 4q weeks.*
  - *Consider radiation therapy or orthopedic consultation if indicated.*
- *Neuropathic pain*
  - *Tricyclic antidepressants: amitriptyline or nortriptyline 10 - 25 mg qhs and titrated up to 150 mg if indicated (choice of drug depends on patient and side-effect profiles).*
  - *Anticonvulsants: gabapentin 100 mg tid titrated up over 3 - 5 days to 300 mg tid and even up to 3 g/d if necessary.*
  - *In developing countries sodium valproic acid or clonazepam is routinely employed due to higher cost with gabapentin.*

- *Others*
  - *Stronger opioids*
  - *Methadone*
  - *iv Lidocaine/mexilitene*
  - *N-methyl-D-aspartate (NMDA) receptor antagonist: ketamine/dextromethorphan*
  - *Interventions: regional, sympathetic blocks*
  - *Neuroaxial medications: opioids, clonidine, local anesthetic.*

Opioid Rotation

- *When pain is uncontrolled despite the use of high opioid doses, when escalation of opioid doses to very high levels makes administration difficult or impractical, or when tolerance or toxic effects develop, rotation to an alternate opioid may be indicated.*
- *Rotation should be done as follows:*

Step 1 Calculate the total daily dose of the opioid.

Calculate the dose of the new opioid using an equianalgesic dose conversion table (See Table 2).
Reduce the new opioid dose by 30%-50% to account for incomplete cross tolerance between opioids.
Establish the regular daily dose of the new opioid.
Order adequate breakthrough dosing.
Continue frequent assessment.

TABLE 2: OPIOID CONVERSION

Conversion from Another Opioid to Morphine (Use table below)
1. Total the amount of opioid that effectively controls pain in 24 hours
2 .Multiply by conversion factor in table below. Five 30% less of the new opioid to avoid partial cross tolerance
3 .Divide by the number of doses/day

Opioid	From parenteral opioid to parenteral morphine	From same parenteral opioid to oral opioid	From oral opioid to oral morphine	From oral morphine to oral opioid
Morphine	1	2.5	1	1
Hydromorphone	5	2	5	0.2
Meperidine	0.13	4	0.1	10
Levorphanol	5	2	5	0.2
Codeine	--	--	0.15	7
Oxycodone	--	--	1.5	0.7
Hydrocodone	--	--	0.15	7

*Conversion to methadone is done with caution. Methadone is 10-15 times more potent than morphine, hence methadone usage has learning curve associated with it, and should be done by physicians familiar with its potency and pharmacokinetics.

Sustained Release (SR) Opioids

- *Because the active drug is gradually released from SR opioids, SR opioids can be taken at convenient, extended intervals: q12h or q24h for morphine-SR, q12h for hydromorphone-SR and oxycodone-SR. Infrequently, q8h dosing may be necessary in some patients. Transdermal fentanyl patches are to be changed q72h.*
- *Patients with stable controlled pain achieved with minimal breakthrough dosing are likely candidates for SR opioids.*
- *In opioid-naïve patients, initial dosing with IR drugs allows rapid, safer upward titration. Changing to an SR opioid can be accomplished when relative pain control and dosing stability are achieved.*
- *Because unstable pain may prove difficult to manage with SR opioids, changing to IR opioids is indicated.*
- *A patient with renal insufficiency is at greater risk for metabolite accumulation when taking SR opioids.*
- *Changing from an IR opioid regimen to SR opioids should be done as follows:*
  Calculate the total daily dose of the IR opioid.
  Divide the dosage into the desired dosing intervals and prescribe the SR opioid.

Prescribe adequate breakthrough dosing.

- *When starting an SR opioid, order the initial dose 4 hours after the final dose of the IR opioid and provide sufficient breakthrough coverage.*
- *Escalation of the SR opioid may be necessary due to the development of opioid tolerance or progressive disease. The amount of increase is usually based on the total breakthrough dosing used.*
- *Situations where SR opioids may need to be discontinued include unstable pain, opioid toxicity, and renal insufficiency.*
- *Changing from an SR opioid regimen to IR opioids should be done as follows:*
  Step 1: Calculate the total daily dose of the SR opioid.
  Step 2: Calculate the q4h and breakthrough dosing based on the SR opioid daily total.
  Step 3: Start the IR opioid 12 hours after the last SR opioid dose.
  Step 4: Order adequate breakthrough dosing to cover the transition interval.

Transdermal Fentanyl

For a patient who is unable to take oral medications and does not have a gastric tube in place for access to the enteral route, transdermal fentanyl offers a convenient, generally well-tolerated alternative. This is a slow-onset, long-lasting opioid system that offers convenience and usually satisfactory pain control in patients. Titration in acute situations is difficult with patch. In such situations fentanyl patch should be discontinued, replacing with intravenous opioid after accounting for equianalgesic conversion.

- *Changing from another opioid to transdermal fentanyl should be done as follows:*
  Step 1: Calculate the total daily dose of the current opioid.
  Step 2: Calculate the equianalgesic 24-hour morphine parenteral dose.
  Step 3: Determine the equivalent transdermal fentanyl dose using the fentanyl conversion table (Table 3).
  Step 4: Continue the previous opioid for 8 -12 hours after applying the patch (Slow onset).
  Step 5: Order adequate breakthrough dosing based on the calculated daily total.
  Step 6: Change the patch q72h (rare patients will need a change q48 - 60h).
- *Discontinuing transdermal fentanyl should be done as follows:*
  Step 1: Calculate the equivalent dose of the new opioid.
  Step 2: Calculate the scheduled interval and breakthrough dose of the new opioid.
  Step 3: Remove the patch and start the new opioid 12 hours later (the half-life of ransdermal fentanyl is more than 12 hours after discontinuation).
  Step 4: Order adequate breakthrough dosing to cover the patient in the interval.

Transmucosal Fentanyl

Oral transmucosal fentanyl provides rapid systemic dosing via absorption through oral mucosa. It likely will have a significant role in treating both constant and breakthrough cancer pain as clinical evidence regarding its efficacy and cost-effectiveness accumulates. It is not yet available in developing countries.

TABLE 3: CONVERSION TO TRANSDERMAL FENTANYL

a) Determine 24-hour morphine equivalent requirement using table below

b) Select the mcg per hour dose according to the ranges listed below. For dosage requirements >100 mcg per hour multiple patches can be used.

c) Patch duration=72 hours. To titrate the dose effectively, prescribe a PRN dose of morphine or other opioid especially during the first 12 hours. The patch will take 18 hours to peak. Increase the dose based on the additional amount of opioid required during the 72 hour period.

Parenteral Morphine (mg per 24 hours)	Transdermal Fentanyl Equivalent
8-22	25
23-37	50
38-52	75
53-67	100
68-92	125
83-97	150

Methadone

A synthetic opioid and NMDA antagonist, methadone is emerging as a potent weapon in treating cancer pain of multiple etiologies. Its characteristics include excellent absorption, high lipid solubility, high potency, long but unpredictable half-life, lack of known metabolites, decreased opioid cross-tolerance, and low cost. Its unique pharmacodynamic and pharmacokinetic properties contribute to its unique ability to relieve pain that is unresponsive to other potent opioids. One caveat: methadone's potency and long half-life can also make it somewhat finicky to manage, especially when converting from another opioid. Thus, cautious observation during titration is warranted. ts equianalgesic ratio should also be noted. Recent studies indicate that methadone is 10-15 times more potent than morphine, hence, caution should be observed when switching to methadone from other opioids. Most drug interactions with methadone involve inducers or inhibitors of the cytochrome p450 system. Hence, caution is needed when drugs sharing the same metabolic pathway are used in conjunction with methadone. For example, desipramine plasma levels increase when it is used with methadone, the metabolism of the antiretroviral agent zidovudineis inhibited and its clearance is delayed when used with methadone, and serotonin-selective re-uptake inhibitors produce increased serum levels of methadone in rapid metabolizers.

Methadone has emerged as a very useful drug in intractable pain states, especially when the pain is both somatic and neuropathic. However one must be familiar with its dosage and equianalgesic ratio as well as have an idea about interactions between it and other drugs.

OPIOID TOLERANCE AND DEPENDENCE ISSUES

As mentioned earlier, cancer pain is often undertreated for various reasons, including misinformed attitudes about tolerance and dependence. Patients may be fearful of becoming addicted to opioids, and physicians may be reluctant to prescribe opioids for that reason. Yet, to provide rational pain management to cancer patients, the clinician should be aware of the basic facts about and differences between opioid tolerance, physical dependence, and psychological dependence ("addiction").

Opioid Tolerance

On one hand, the progression of disease in advanced cancer patients typically leads to increased pain that requires increased opioid dosing. On the other hand, the increasing doses of an opioid necessary to yield the same analgesic effect as previous lower doses may indicate the development of tolerance. The mechanism of this normal physiological phenomenon may be alterations at the opioid receptor level or changes in opioid metabolism. The development of tolerance varies greatly among patients and opioids. Because cross-tolerance among opioids is incomplete, alternative opioids can be used if tolerance becomes problematic or if the patient experiences dose-limiting side effects. Hence, the development of tolerance may be an indication for opioid rotation. It is ill advised to reserve the use of opioids for later in the progression of disease due to concern about tolerance.

Physical Dependence

Physical dependence is a common normal pharmacophysiological effect of chronic opioid (and also steroid and beta-blocker) use. The body simply becomes accustomed to the medication. Upon abrupt reduction or discontinuation of the opioid or administration of an opioid antagonist, the patient will display signs of an abstinence or withdrawal syndrome agitation, tremulousness, fever, diaphoresis, mydriasis, tachycardia, and muscle and abdominal cramping. If reduction or cessation of opioids is indicated, the opioid dose should be tapered at the rate of 10 %- 20% each day.

Psychological Dependence ("Addiction")

Psychological dependence ("addiction") is the psychopathological compulsion to use a substance, resulting in physical, psychological, or social harm to the user, and compulsive persistent use despite the harmful effects. Substantial evidence confirms that cancer patients taking opioids appropriately for cancer pain are at virtually no risk for developing psychological dependence.

Pseudoaddiction

Pseudo-addiction is a condition characterized by drug-seeking behavior caused by unrelieved pain. This condition may be iatrogenic because of the undertreatment of pain. Improved assessment and rational pain management regimens should solve this problem.

NONPHARMACOLOGICAL TREATMENT

- *Stimulation or ablation*
- *Nerve blocks*
- *Physical therapy*
- *Psychological techniques*
- *Acupuncture.*

PRINCIPLES OF ANESTHETIC PROCEDURES IN CANCER PAIN

- *Usually reserved for patients whose pain fails extensive pharmacological trials*
- *Should fail to show dose response or dose-limiting side effects, which are resistant to treatment*
- *Neurolytic or destructive procedures are usually done in terminal patients due to adverse effects.*

Useful Anesthetic Procedures

- *Celiac plexus/splanchnic block for abdominal visceral pain, e.g., pancreatic cancer pain*
- *Subarachnoid neurolytic block for extremity and thoracic wall pain in terminally ill patients*
- *Epidural/intrathecal opioids ± LA, e.g., for neuropathic or plexopathy pain spell out LA*
- *Cordotomy for lower extremity intractable pain*
- *Vertebroplasty (injection of cement into a vertebral body) for metastatic spine pain involving one or two vertebrae.*

PHYSICAL THERAPY

Physical therapy modalities, such as massage, ultrasound, hydrotherapy, electroacupuncture, and trigger-point injection, are indicated for musculoskeletal pain, any of which may enhance exercise tolerance in a patient undergoing rehabilitation. Skillful soft-tissue manipulation is probably underutilized.

PSYCHOLOGICAL TECHNIQUES

Cancer patients may benefit enormously from using psychological techniques such as imagery, hypnosis, relaxation, biofeedback, and other cognitive or behavioral methods.

CONCLUSION

The information in this chapter should provide fundamental concepts and information that enable the reader to properly assess pain and institute rational, effective basic management regimens. The stepwise progression of pain management described here facilitates titrating the regimen to appropriately match the stage of pain and concomitant symptoms, and it allows the clinician to approach pain and concurrent problems proactively. Concise pain management algorithms can be found in the M. D. Anderson Cancer Manager intranet system.

Palliative Pearls

- *Pain is a multidimensional experience that requires multidimensional assessment.*
- *Because pain and other symptoms can change rapidly in the advanced cancer patient, regular and frequent assessment is necessary.*
- *Ask the patient about his or her pain, and believe what his or her reports.*
- *Reassure the patient and family that most pain can be relieved.*
- *Reassure the patient and family about their concerns and fears regarding opioids.*
- *Explain to the patient the differences between physical dependence, addiction, and tolerance.*
- *Almost all patients with advanced cancer require treatment until death. Thus, concerns about dependence and addiction are irrelevant.*
- *Encourage normal activity to the fullest extent possible.*
- *Treat pain promptly and aggressively.*
- *Rational pain management tailors the regimen to the type and intensity of pain.*
- *Regular atc opioid administration with adequate breakthrough dosing and adjuvants as required and proactive antiemetic and laxative regimens is the hallmark of rational and effective pain management in the cancer patient.*
- *Optimize opioids before adding adjuvants.*
- *Because opioid conversion tables are inexact, patients should be observed carefully whenever regimen changes are made.*
- *Consider nonpharmacological options to control pain, such as anesthetic and neurosurgical approaches, in intractable pain syndromes where the risk:benefit ratio favors benefit.*
- *Beware of overzealous use of opioids in the patient who is experiencing delirium or somatization.*
- *Benzodiazepines and phenothiazines are questionable adjuvants. They may cause oversedation and confusion and do not address pain.*
- *Beware of the pitfalls of polypharmacy.*
- *Treating the patient who suffers from total pain (nociception, psychological distress, and spiritual distress) means treating the whole patient (body, mind, and spirit).*

"Pain is a more terrible Lord of mankind than even death itself." Albert Schweitzer

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9 Other Problems in Patients with Cancer

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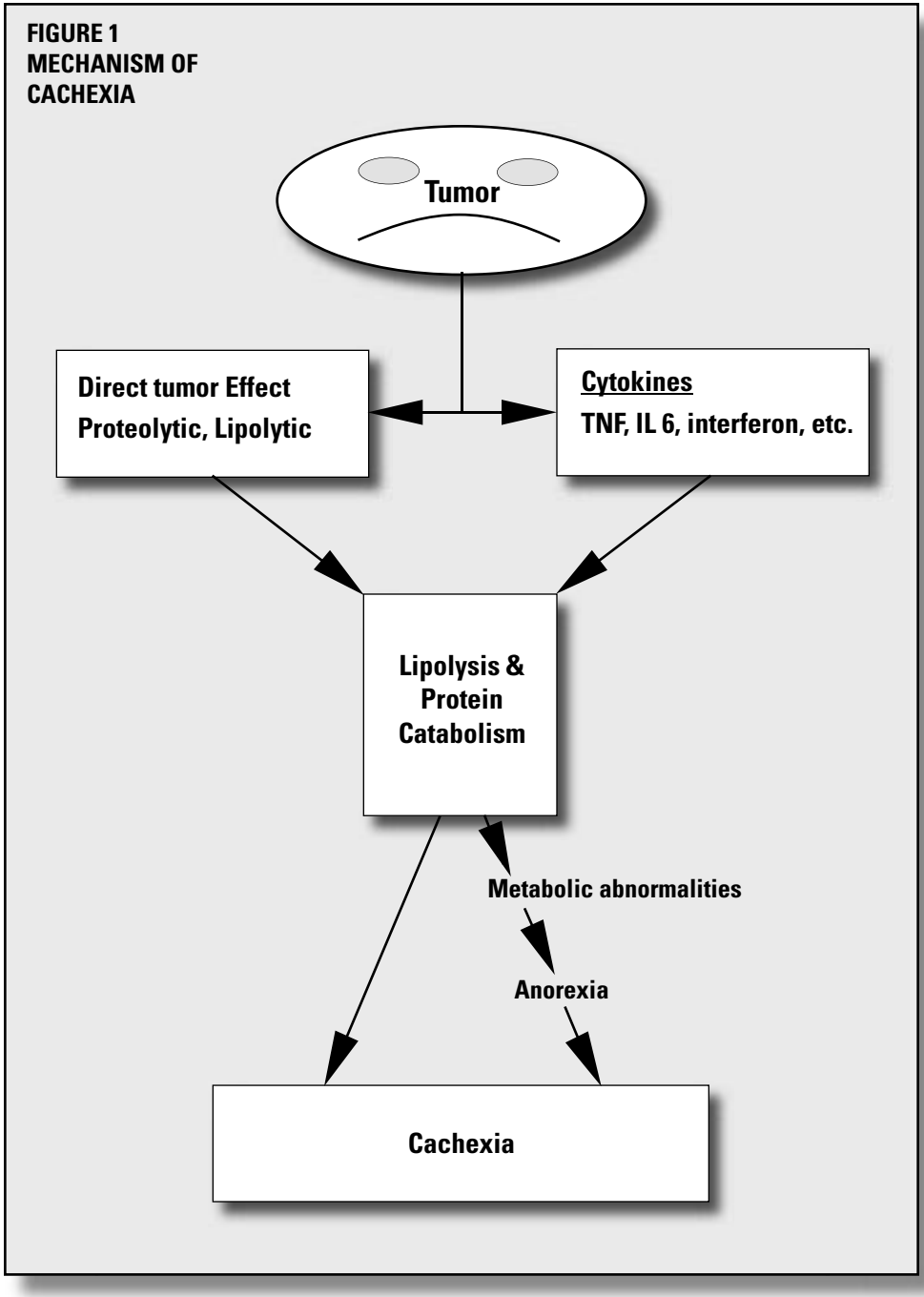
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ANOREXIA AND CACHEXIA

Anorexia, cachexia, or both occur in 80%-90% of patients with advanced cancer. These problems of diminished appetite and weight loss accompanied by wasting of muscle mass often occur in constellation with severe lethargy, fatigue, and generalized weakness known, as asthenia. This syndrome of anorexia/cachexia/asthenia impacts the patient and family and challenges the health care team. Patients with this syndrome have impaired quality of life and prognosis, and they are more prone to have side effects or respond poorly to treatment. Cachexia tends to occur more frequently in patients with solid tumors (the exception being breast cancer), children, and elderly patients. The symptom triad worsens concomitantly with disease progression.

The etiology of anorexia/cachexia/asthenia is multifactorial (see Figure10). The main cause in most patients is profound metabolic change due to tumor by-products and host cytokines, i.e., tumor necrosis factor, cachectin, and interleukin. These mediators alter carbohydrate, lipid, and protein metabolism, leading to lipolysis with loss of fat mass and proteolysis with loss of body protein and muscle wasting as well as asthenia and anorexia. Decreased food intake also contributes to cachexia, particularly in patients with nausea, dysphagia, bowel obstruction, or constipation. Other contributing factors may include food aversion, depression, or apathy.

FIGURE 1
MECHANISM OF CACHEXIA



Clinical Assessment and Diagnosis

Clinical assessment and diagnosis should include a careful history focused on nutritional issues and a physical examination, especially of the alimentary tract, which is usually enough to make the diagnosis. As stated in chapter 7 assessment of other symptoms is essential.

A simple diagnostic indicator is the following: a 5-lb weight loss in the previous 2 months and/or an estimated daily caloric intake of <70 calories /kg of body weight.

Management

The initial approach to management includes attempting to remove the cause, but this is rarely possible. Mainstays of therapy include improving the quality of life by general measures aimed at controlling concurrent symptoms and stimulating appetite. A nutritionist can help assess the patient's nutritional status and advise dietary options to maximize nutritional intake.

Pharmacological Symptom Control and Appetite Stimulation

- *Treat chronic nausea or early satiety with GI motility agents (e.g., metoclopramide 10 mg q4h, cisapride 10 mg qid).*
- *Stimulate appetite with progestational agents, corticosteroids, cannabinoids, or adjuvant agents:*
  - ***Progestational agents** (e.g., megestrol acetate 40-120 mg po qid) will improve the appetite in up to 80% of patients and induce weight gain in many of them. Indeed, these agents are the only ones that have a clearly demonstrated ability to induce weight gain (mostly due to increased fat). Weight gain occurs only after several weeks of treatment at high doses (minimum 160 mg tid). However, symptomatic improvement (increased appetite and energy level) can be seen with lower doses in less than 1 week. Appetite stimulation with these agents typically lasts longer than with corticosteroids, and a concurrent decrease in nausea is a welcome benefit. Even though they produce fewer side effects than corticosteroids, progestational agents increase the risk of thromboembolic phenomena and should be avoided in patients with a history of deep venous thrombosis, pulmonary embolism, or severe cardiac disease.*
  - ***Corticosteroids** (e.g., dexamethasone 4-10 mg po/iv/sc bid) may stimulate the appetite temporarily before losing effectiveness after a few weeks, and prolonged use is not recommended. The improved appetite comes without concomitant weight gain. Positive effects include abatement of nausea and an improvement in the general sense of well-being. A successful 1-week trial of dexamethasone may be continued and tapered slowly over ensuing weeks. More rapid tapering can be undertaken if appetite remains unimproved during that first week. The most common side effects include abnormal glucose tolerance, infections, and dysphoria or mania.*
  - ***Cannabinoids** May be effective appetite stimulants and may produce concurrent antiemetic effects, but they may also produce potential problematic side effects in the CNS.*
  - ***Antidepressants** Tricyclics, Selective Serotonin Reuptake Inhibitors (SSRI) may be of benefit in improving appetite in patients with depressive symptoms.*

Enteral and Parenteral Nutrition

Enteral and parenteral nutrition therapies are too aggressive and thus inappropriate for most patients with advanced cancer. These therapies do not enhance response to antineoplastic therapy or significantly abate its toxicity, and they do not improve survival or quality of life. These types of therapy are also expensive, may have serious side effects (e.g., septicemia, electrolyte and glucose imbalances), and are uncomfortable for patients and families to maintain at home or in small hospitals. Their use should be limited mostly to patients in whom there is a clearly defined starvation component to cachexia, such as severe dysphagia related to head and neck or esophageal cancer, bowel obstruction related to slowly growing tumors, or other special situations.

Palliative Pearls

- *Improve the patient's and family's understanding of the metabolic abnormalities. If they understand that anorexia is more a result of the cachexia syndrome than the cause of the problem, they will be less likely to force-feed the patient and bring on the resulting nausea and psychological distress.*
- *Explain that aggressive enteral or parenteral nutrition will not have a significant impact on well-being or survival.*
- *Encourage the eating of favorite foods for the comfort and enjoyment they give as their nutritional value may be of limited importance.*
- *Explain potential problems with and the lack of benefit of parenteral nutrition modalities. This will help the patient and family make an informed decision about their use.*

CANCER FATIGUE

Fatigue, or the physical or mental weariness resulting from exertion, is transient in most of us. For patients with advanced cancer, however, fatigue may be a severe symptom that either decreases their capacity for physical and mental work or renders them completely unable to function normally. In the context of the other symptoms that impact the advanced cancer patient, the burden of fatigue results in lack of energy, malaise, lethargy, and diminished mental functioning that profoundly impairs the patient's quality of life. Patients may experience fatigue early in the course of their disease and may even have treatment-related exacerbations of the problem. Virtually all patients with advanced cancer will experience fatigue, especially as the disease progresses towards end stage. The presence of fatigue may also magnify other symptoms affecting the patient.

As with other symptoms in patients with advanced cancer, the causes of fatigue are multifactorial and interrelated. These include problems related to the cancer itself, treatment side or toxic effects, underlying systemic pathophysiological disorders, and other causes.

The severity of fatigue can be measured on a scale of 0 - 10 (where 0 equals no fatigue and 10 equals the worst fatigue imaginable) or by other numeric or verbal rating scales. The best assessment of fatigue is multidimensional and considers the impact of fatigue on activities, function, and quality of life. Historic assessment includes the course of fatigue and related factors and their impact upon the patient. Certainly, underlying cancer factors and treatments must be considered, as must other

systemic pathophysiological problems and psychological distress. Laboratory investigations and imaging studies should be based on indications derived from the patient history and physical findings.

Management of Fatigue

As with other problematic symptoms in advanced cancer patients, management of fatigue should address possible underlying etiologies as well as the patient's expression of symptoms.

Step 1: Treat underlying problems.

- ***Pain****: (See Chapter 8, Cancer Pain)*
- ***Depression, anxiety, stress, or sleep disturbances***
- ***Dehydration***
- ***Anorexia/cachexia***
- ***Medications:*** *Simplify medication regimens*
- ***Infection:*** *Give appropriate antibiotics*
- ***Anemia:*** *Transfuse packed red blood cells, or administer epoetin alpha 10,000 U sc three times weekly as indicated*
- ***Immobility:*** *Prescribe activity as tolerated*

Step 2: Administer pharmacological agents

- ***Megastrol acetate and corticosteroids:*** *There is reliable evidence that megastrol acetate (160 mg tid) and the corticosteroid dexamethasone (4 - 8 mg bid) may mitigate fatigue in advanced cancer patients*
- ***Psychostimulants:*** *Psychostimulants (e.g., methylphenidate 5 - 10 mg in the morning and 5 - 10 mg at noon) may be useful in the treatment of fatigue related to concurrent problems such as depression, hypoactive delirium, or drowsiness due to opioids*
- ***Antidepressants:*** *SSRIs or Tryciclic Antidepressants (TCAs) may improve energy levels in some fatigued patients, though their benefit is unproven*

Palliative Pearls

- *Fatigue is an almost universal symptom in patients who have advanced cancer.*
- *Treatment of fatigue in advanced cancer patients will likely be more difficult than in patients with earlier stage disease.*
- *Patients and their families should be educated about the burden of fatigue that accompanies advancing cancer, advised to make efforts to modify activities and rest, and advised to optimize nutrition and hydration as early as possible.*
- *Aggressive treatment of concurrent symptoms may be effective in the mitigation of fatigue.*

DEHYDRATION

The historical standard of medical care mandates that all patients be routinely hydrated. Conversely, traditional hospice models have promoted the concept of not administering parenteral fluid during the terminal phase of incurable illness. Evidence can be found to support both approaches. However, it is important to remember that dehydration may cause problems that exacerbate patient suffering, such as confusion and renal failure, resulting in accumulation of active drug metabolites. Accumulation of opioid metabolites in particular can cause nausea, confusion, restlessness, myoclonus, seizures, and

even hyperalgesia. Dehydration also increases the risk of pressure ulcers. Thus, adequate hydration is important both as a comfort measure and in symptom control.

Assessment of Dehydration

- *Symptoms and signs of dehydration include the following:*
  - *Fatigue*
  - *Postural hypotension*
  - *Confusion/delirium*
  - *Constipation*
  - *Dry mouth/thirst (this is more frequently due to opioids, other drugs, and oral complications of cancer rather than dehydration).*
- *Physical examination may reveal the following signs of dehydration:*
  - *Lethargy or confusion (especially with severe dehydration)*
  - *Poor skin turgor*
  - *Decreased jugular venous pressure*
  - *Dry mucous membranes.*
- *Laboratory evaluation may reveal the following:*
  - *Decreased urine sodium*
  - *Elevated hematocrit reflecting hemoconcentration*
  - *Hypernatremia*
  - *Elevated BUN and normal creatinine in early dehydration*
  - *Elevated BUN and elevated creatinine indicating renal deterioration in late dehydration.*
- *Evaluation of fluid intake and output will reveal the diminished output typical of hypovolemia.*

Decision-Making Regarding Hydration

- *Consider the symptoms of dehydration in your patient. In some cases, the relationship between a given symptom (i.e., asthenia or confusion) and dehydration can only be established through a short therapeutic trial of hydration.*
- *Consider the disadvantages of hydration: , issues of care at home or in rural areas, cost, worsening of pre-existing congestive heart failure CHF, etc.*
- *Choose the most effective and simplest hydration system, and measure the expected outcome.*
- *If no improvement is observed, or if the patient or family feels that the toxicity or discomfort is worse than the potential benefit, discontinue.*

Methods of Hydration

When the decision is made to hydrate the patient, various options are available. Patients able to take fluids orally should do so, as this is the preferred route. However, patients who are unable to maintain oral fluid intake should receive parenteral hydration. Patients with patent iv lines can be hydrated by that route unless it becomes problematic. Then, the preferred route becomes subcutaneous administration of fluids, i.e., hypodermoclysis or "clysis."

Fluids may be administered via clysis either as a bolus or continuous infusion. Advantages of clysis include the following:

- *Easy site access*
- *Suitability for home administration because of its ease and safety*

- *Ability to use these sites for up to 7 days*
- *Easy stoppage of clysis infusion and disconnection to facilitate patient mobility*
- *Freedom of limbs and freedom from iv poles or pumps when clysis is administered via daily boluses.*

Hypodermoclysis can be initiated to fit varying clinical situations, including the following:

- *Rehydration:*
  Fluid type: normal saline
  Rate: 70-100 mL/hour via continuous infusion.
- *Fluid maintenance or augmentation:*
  Fluid type: two thirds dextrose and one third normal saline or 5% dextrose and ½ normal saline nuous infusion),

1000 mL by gravity overnight (overnight clysis), or
500 mL bolus bid, with each bolus infused over 1 hour (bolus).

Hyaluronidase may facilitate fluid absorption, but it is not necessary in most patients to effectively administer fluid subcutaneously. If significant amounts of fluid leak from the sc infusion site, 150 U hyaluronidase can be added to each liter of fluid or as an injection to the sc site once a day. Though reactions to hyaluronidase are uncommon, mild redness may occasionally be seen around the infusion site. If the patient is comfortable, the clysis can be continued. More severe reactions, although rare, are characterized by swelling, redness, and pruritus. Hyaluronidase should be discontinued in such cases.

Proctoclysis:
Proctoclysis is a simple and inexpensive, alternative method of hydration, that may be helpful in situations where resources are limited. It utilizes the colon's intrinsic ability to absorb water. To perform proctoclysis a 22 French nasogastric catheter is inserted about 40cm into the rectum and is used to infuse normal saline or tap water. Rates of infusion of 100-400mL/h have been reported. Following the infusion of the desired total daily volume of water, the catheter is then removed and reinserted the following day. An assessment of comfort showed that this technique is well tolerated. Family members have successfully administered proctoclysis in the home. This method may be especially helpful in situations where technical difficulties make IV or subcutaneous infusion difficult. Such settings may include developing countries, a rural setting, or situations where nursing care is limited.

Ongoing Reassessment of Treatment

The patient's clinical status should be routinely monitored and infusion volumes adjusted as needed to prevent overhydration. Overhydration in terminally ill patients is mostly due to decreased body mass, vascular volume, insensible losses, and elimination of free water. Fluid volumes of l-1.5 L/day are usually sufficient to maintain adequate urine output and normal laboratory values in these patients. The assessment measures mentioned above should be used.
If at end stage it becomes appropriate to discontinue hydration, medication regimens, especially opioids, may need to be adjusted to preclude accumulation of metabolites.

Palliative Pearls

- *Not giving the patient water can be a source of symptom distress. Think of water as a "medication" and "comfort aid." The volume of hydration should be titrated frequently while attending to the clinical response rather than using a cookbook approach.*
- *Terminally ill patients generally require less fluid than less gravely ill patients do.*
- *Edema is not a good indicator of hydration status in patients with advanced cancer. Edema more often is a result of tumor blockage accompanied by impaired venous or lymphatic drainage or of cachexia-related hypoalbuminemia.*
- *Thirst or dry mouth is not a reliable indicator of dehydration but more frequently results from opioid therapy, other drugs (i.e., tricyclics), oral candidiasis, viral infections, or mouth breathing. It can be controlled with ice chips, good oral hygiene, and occasionally pilocarpine tablets in patients with radiation- and/or opioid-induced xerostomia.*

DELIRIUM

Delirium is an acute confusional state that results from diffuse organic brain dysfunction.

As many as 80% of patients with advanced cancer develop delirium during the last week of life. Many of these patients also experience several prior episodes of delirium that completely resolve. Approximately 30% of delirium episodes are reversible. Delirium shortens the survival of cancer patients, makes the assessment of pain and symptoms difficult, and is a main cause of distress among patients, family members, and health care providers. Diagnosis of delirium is a commonly missed, and its early symptoms, such as anxiety; insomnia, and mood changes, may be treated with anxiolytics and antidepressants, which may worsen the delirium.

Clinical Presentation

Delirium is due to global brain dysfunction. Its main diagnostic criteria are as follows:

- *Acute or subacute onset and fluctuating course*
- *Variable sensorium accompanied by impaired alertness, orientation, cognition, and attention (sundowning)*
- *Psychomotor abnormalities accompanied by agitation, somnolence, hallucinations, or delusions.*

Clinical subtypes of delirium include the following:

- *Hyperactive: confusion + agitation ± hallucinations ± delusions ± myoclonus ± hyperanalgesia (may be mistaken for anxiety or EPS)*
- *Hypoactive: confusion + somnolence ± withdrawal (may simulate depression)*
- *Mixed: symptoms of both hyperactive and hypoactive delirium.*

Careful attention must be given to the differential diagnosis, which can be complex.

Patients with hypoactive delirium are frequently diagnosed with depression. However, while delirium is common in advanced cancer palliative care patients (up to 80%), depression occurs less frequently (10 - 25%). On the other hand, patients with mild delirium often have depressive symptoms. Another

confounding diagnosis to be considered is dementia, which is unlikely unless the patient has been previously diagnosed with that problem or is older than 80 years of age.

Causes of Delirium

Because the etiology of delirium is often multifactorial, a specific cause occasionally remains unidentified. However, this should not deter the health care professional from looking for underlying causes as many cases of delirium are reversible by identifying and treating those problems.

Management of Delirium

Step 1: Assess the patient.

- *Maintain a high index of suspicion. Use screening tools such as the MMSE, Clock-making, or the Memorial Delirium Assessment Scale.. These screening tools should be used even in patients with no overt signs of delirium to make an early diagnosis.*
- *Ask the patient specifically about hallucinations (they are more often tactile than visual) and delusional thoughts. Patients frequently do not volunteer information about these symptoms.*
- *Look for clinical signs of sepsis, opioid toxicity, dehydration, metabolic abnormalities, or other potential causes of delirium.*
- *Order appropriate tests, such as a complete blood count, electrolytes, calcium (with albumin), blood urea nitrogen (BUN) and creatinine, chest x-ray, O2 saturation, and others as indicated.*

Step 2: Treat the underlying cause.

- ***Opioid toxicity:*** *rotate opiods (see Chapter 8 on Cancer Pain).*
- ***Sepsis:*** *start appropriate antibiotics after discussing treatment options with the patient and the patient's family.*
- ***Drugs:*** *discontinue all possible offending medications, especially TCAs, benzodiazepines, certain antiemetics and antibiotics, and cimetidine.*
- ***Dehydration:*** *start hypodermoclysis with normal saline at 60 - 100 mL/hour, or alternatively give boluses of 500 cc administered over 1 hour three or four times daily. If an iv line is already established, hydration can easily be administered throught it.*
- ***Hypercalcemia:*** *treat with bisphosphonates.*
- ***Hypoxia:*** *treat the underlying cause and administer oxygen.*
- ***Brain tumor or metastasis:*** *consider high-dose corticosteroids.*

Step 3: Treat the symptoms of delirium.

- ***Agitation/hallucinations:*** *To treat agitation, start haloperidol 2 mg po/sc q6h and 2 mg q1h po/sc prn. To bring severe agitation rapidly under control, it may be necessary to give haloperidol more frequently initially (e.g., 2 mg q15 - 30 min sc/po prn during the first hour and q1h prn thereafter). It is important to bring agitated delirium under control as rapidly as possible prevent patient, family, and staff distress. Once symptoms are under control, start reducing the dose to the minimal effective dose as soon as possible. Sometimes infusion of haloperidol or more sedating antipsychotic medications (such as chlorpromazine perphinazine) may be required, at which time we encourage palliative care or psychiatric consultation. On rare occasions, aggressive sedation may be required. When indicated, start a continuous sc infusion of midazolam at 1 mg/hour and titrate according to clinical response.*

Step 4: Counsel the patient's family and health care professionals.

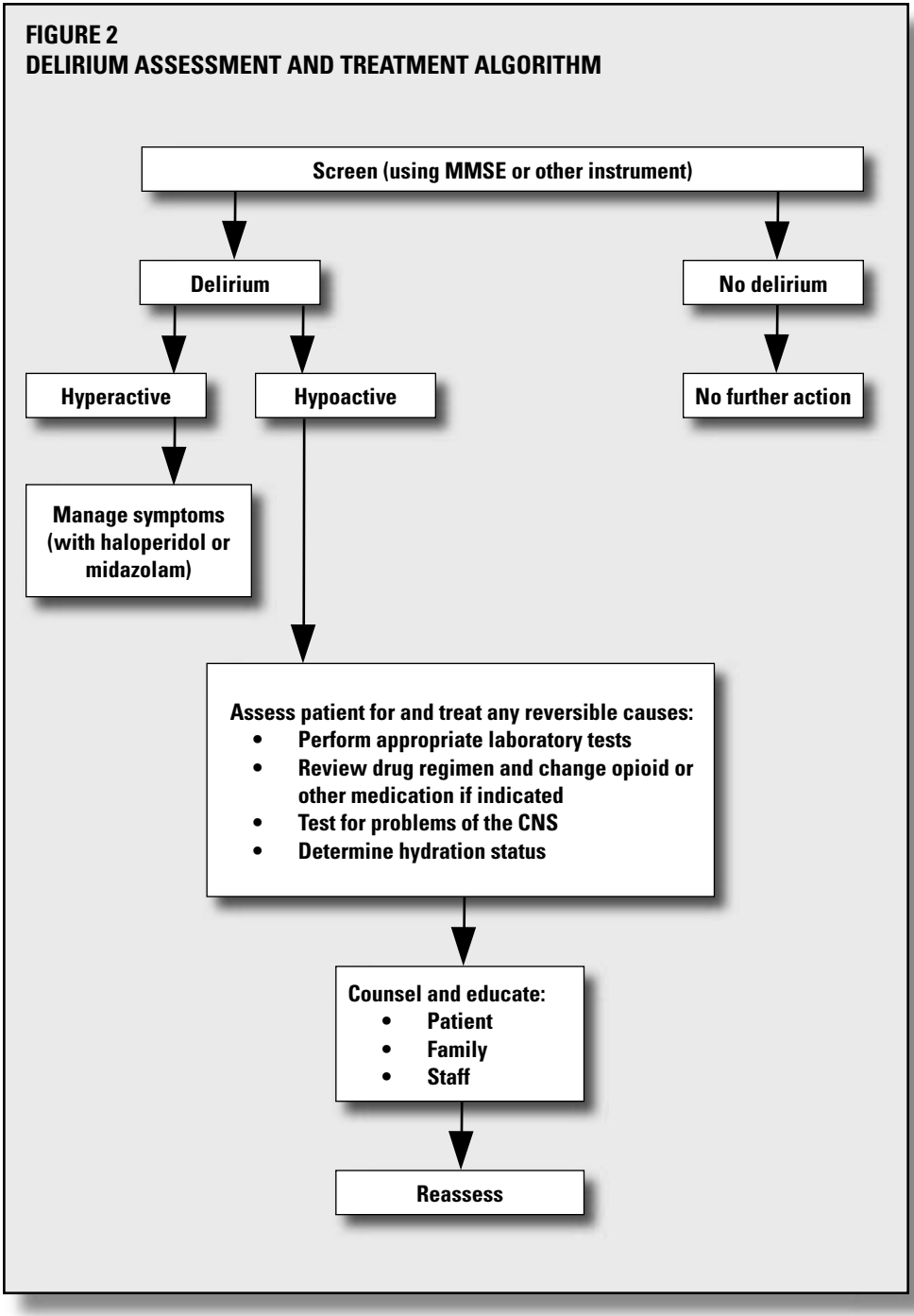
- *Confusion and agitation are expressions of brain malfunction and not necessarily of discomfort or suffering. Disinhibition is one of the main components of delirium and may result in two possibly distressing phenomena:*
  - *Dramatic expression of previously well-controlled physical symptoms by grimacing or moaning: Family or staff may interpret this as aggravation of symptoms rather than merely increased expression. In addition to observer distress, this can lead to the patient's excessive use of opioids and/or adjuvant drugs and the accompanying potential for exacerbation of delirium.*
  - *Unreasonable requests of family or staff (e.g., "I want to go home now."): If these requests are not immediately addressed, the patient may become hostile. Unless appropriately explained to the patient's family, this disinhibited behavior may be quite distressing to them.*
- *Most patients will have little or no recollection of their own symptoms (i.e., hallucinations, delusions) after the episode has subsided.*
- *The aim of palliative treatment is comfort rather than prolonged life.*

A simple clinical algorithm for assessing and treating delirium is shown in Figure 2.

Palliative Pearls

- *Because delirium is common in palliative care patients, be alert to its possibility.*
- *Depression and dementia may complicate the differential diagnosis of delirium.*
- *Hypoactive delirium may be wrongly diagnosed as depression and treated inappropriately with antidepressants.*
- *Agitated delirium may be wrongly assessed as anxiety or insomnia and treated with benzodiazepines.*
- *Mistakenly interpreting agitation and the accompanying grimacing and moaning of delirium as signs of poor pain control may result in inappropriately increasing opioid doses.*
- *Drugs that could be causing or aggravating delirium should be discontinued.*
- *Urinary retention and constipation are factors capable of aggravating agitation.*
- *Previously unrecognized cognitive dysfunction may manifest itself as delirium during the course of cancer or palliative treatment.*
- *Patients may have episodic lucid intervals marked by clearing of their sensorium.*
- *Intractable delirium may herald impending death.*

FIGURE 2
DELIRIUM ASSESSMENT AND TREATMENT ALGORITHM



DEPRESSION

Emotional distress is a normal response to the catastrophic event that a cancer diagnosis represents, especially if the cancer is not curable. For most patients, this distress is transient, and the patient and family are able to adapt with time and general supportive care. However, approximately 25% - 35% of cancer patients will suffer from mild to moderate depression, and 5% - 10% will suffer from severe depression.

The diagnosis of depression is often difficult to ascertain in cancer patients. The most obvious problem is that sadness and grief are expected responses to the diagnosis of cancer and at various transition points in the disease. Another is that the physical signs of depression (such as fatigue, anorexia, sleep disturbance, etc.) may be attributable to the disease itself. Finally, many of the medications used by cancer patients may cause depression and/or its physical symptoms.

The best starting point for assessing mood dysfunction in cancer patients is a careful history and physical examination and a simple question: "Have you recently been bothered by feeling down, depressed, or hopeless?" Another useful question is: "Have you often been bothered by having little interest or pleasure in doing things?" The first question targets depressed mood, while the latter is an indicator of anhedonia.

Management of Depression

Step 1: Perform a thorough initial assessment:

- *Note previous depressive episodes*
- *Consider the patient's family history of depression or suicide*
- *Ascertain any current or prior substance abuse (see CAGE questionnaire, Chapter 7)*
- *Directly ask the patient whether he or she is contemplating suicide*
- *Rule out delirium*

Step 2: Facilitate effective communication:

- *Anticipate and allow sufficient time for breaking bad news to the patient (this usually works better near the end of the day)*
- *Make follow-up assessments of fragile patients more frequent (this is more effective than lengthy but infrequent assessments)*
- *Get the setting right (i.e., make sure the patient is comfortable and accompanied by family/friends)*
- *Provide information to the patient directly and without jargon*
- *Respond to the patient's emotions with empathy, but avoid giving unrealistic expectations. A useful phrase for empathizing with the patient and acknowledging disappointing facts is to simply state, "I wish things were different"*

Step 3: Consider psychological interventions:

- *Know the patient's psychological counselor if he or she has one and send the counselor a referral note summarizing the patient's cancer status and other significant clinical findings*
- *Allow the patient a safe opportunity to express his or her concerns and fears about cancer and the end of life. If some of the patient's family members hinder such expression, consider a split counseling session*

- *If psychological interventions (such as support groups, relaxation exercises, cognitive-behavioral therapy, and problem-solving therapy) are available and feasible for your patient, encourage participation in them and provide specific referrals or contact information*

Step 4: Evaluate the patient for significant major depression:

- *Look for profound levels of worthlessness, guilt, anhedonia, and hopelessness*
- *Ask about suicidal ideation. If the patient has active suicidal ideation, refer the patient to a behavioral health professional*
- *Consider possible medical causes of depression:*
  - *Hypercalcemia, thyroid dysfunction*
  - *Beta-blockers, steroids, anticonvulsants, other drugs*
  - *Poorly controlled pain.*

Step 5: Use antidepressants appropriately.

- *Antidepressants may be used to manage mild, moderate, or severe depressive symptoms. However, their optimal use in cancer patients is still poorly defined. Every known antidepressant increases neurotransmission of serotonin, norepinephrine, and/or dopamine. Distinct pharmacological mechanisms allow antidepressants to be categorized into one of seven classes: TCAs (such as amitryptyline), norepinephrine/dopamine reuptake inhibitors (such as bupropion), serotonin/norepinephrine reuptake inhibitors (such as venlafaxine), serotonin selective reuptake inhibitors (such as fluoxetine, paroxetine, sertraline, and citalopram), noradrenergic and specific serotonergic antidepressants (such as mirtazapine), monoamine oxidase inhibitors (such as phenelzine), and serotonin antagonist reuptake inhibitors (such as nefazodone). Uncontrolled trials published in the late 1980s and 1990s suggested that antidepressants are also helpful in selected patients. The TCAs, selective serotonin reuptake inhibitors, and even psychostimulants (such as methylphenidate) have been evaluated in cancer populations and shown to be promising.*
- *It is often useful to choose a specific antidepressant whose side effects best suit the patient's situation. For instance, a patient with psychomotor retardation might benefit from a more activating antidepressant, such as methylphenidate or fluoxetine. An agitated and depressed patient may do better with a more sedating drug, such as nortriptyline or mirtazapine.*
- *Cancer patients are often frail, and compared with healthy adults, they often respond to antidepressants at lower therapeutic doses. The following are common initial doses:*
  - *Nortriptyline 25 mg/day (hs)*
  - *Amitriptyline 25 mg/day (hs)*
  - *Fluoxetine 10 - 20 mg/day*
  - *Paroxetine 10 mg/day*
  - *Sertraline 20 mg/day*
  - *Citalopram 20 mg/day*
  - *Venlafaxine 37.5 mg/day*
  - *Mirtazapine 15 mg/day (hs)*
  - *Methylphenidate 5 - –10 mg in the morning and 5 mg at noon.*

Palliative Pearls

- *Most patients will adjust to their disease through adaptive coping strategies.*
- *Depressive disorders in cancer patients can be difficult to diagnose because of the multiplicity of symptoms related to various concurrent problems.*
- *Antidepressants and psychological interventions are effective treatments for depression in cancer patients.*
- *Supportive communication is a cornerstone of depression management and often supplemented with medication.*
- *A sad, withdrawn, depressed-appearing patient may actually have hypoactive delirium, which is often misdiagnosed as depression.*
- *Psychostimulants, with their rapid onset of effect, may be the antidepressants of choice in the terminal cancer patient with a very poor? prognosis.*
- *Psychostimulants are contraindicated for hyperactive delirium or severe anxiety.*
- *Pharmacologica; therapy for anxiety should be used cautiously because of the potential overlapping side effect of sedation when opioids are also used.*

ANXIETY

Anxiety in patients with advanced cancer is often due to stress from the diagnosis itself. The diagnosis may raise fears about anticipated suffering from pain and other symptoms related to treatment and side effects and associated with progressive loss of autonomy leading to death. Many patients with cancer fear that they will become a burden to their loved ones and society admires people who are independent and self sufficient. Thus, loss of control and independence are involved in the fear of becoming a burden.

Episodes of anxiety may occur before and during cancer treatment. Anticipatory anxiety is often seen before tests and procedures or while waiting for test results.

Factors contributing to anxiety include previous or underlying anxiety disorder, unmanaged pain, medical factors. The most common medical factors include abnormal metabolic states, medication side effects, and withdrawal states. Withdrawal states may result from alcohol consumption or use of narcotic analgesics, sedative barbiturates, or benzodiazepines. Patients with head and neck cancer have a much higher risk of withdrawal states than do those with other cancer diagnoses. These patients often have a history of heavy alcohol, tobacco, or drug use.

Akathisia is a common side effect of some antiemetic medications, including metoclopramide, prochlorperazine, and haloperidol. Usually, the onset of akathisia correlates with the use of these medications. The patient's complaints may be particularly distressing and include a sense of internal restlessness and inability to sit still. Severe cases of akathisia have resulted in suicide attempts. Fortunately, discontinuing use of the causative antiemetic usually controls the symptoms of anxiety. Adding a benzodiazepine or antiparkinsonain agent may add to the rapid relief of symptoms.

Assessment of Anxiety

Ask the patient about the following:

- *Bothersome physical symptoms*
- *Psychological distress (fears and concerns)*
- *Previous experiences of anxiety and coping mechanisms*
- *Awareness of condition and prognosis.*

Examination may reveal the patient to be:

- *Diaphoretic, pale or flushed*
- *Hypertensive, tachycardic, tachypneic*
- *Irritable, worried, fearful*
- *Apprehensive, tremulous, jittery, tense, inattentive*
- *Labile, hyperalert, hypervigilant.*

The decision to intervene with behavioral or pharmacological therapies is based on the patient's level of distress and ability of the patient to participate in treatment or function adaptively. For example, if a patient's fear of needle insertion for a biopsy is creating a delay in the procedure, pharmacological or behavioral interventions are appropriate.

When anxiety symptoms do not interfere with treatment or are not intolerable to the patient, no specific interventions are required beyond the reassuring and empathic responses of staff members. Supportive counseling or behavioral techniques may help patients with intolerable anxiety. The rationale for using behavioral therapies is the substitution of more adaptive behavior (i.e., enhanced coping ability) for less adaptive behavior (i.e., anxiety or fear). Relaxation techniques may be beneficial, especially for patients with anticipatory anxiety before tests and procedures. Trained staff may teach these simple techniques, or the patient may use a prerecorded audiotape before and during procedures. Relaxation and self-hypnosis techniques require instruction and practice time; therefore, they are ineffective in some situations. In fact, attempting to instruct patients in these techniques may result in added stress, because it requires a level of concentration that the patient may not be able to achieve. If the patient's anxiety prevents him or her from using thesetechniques, other behavioral interventions, such as slow, deep breathing and distraction from the anxietyproducing event, may be effective. Medication or a combination of behavioral and medication therapies should be considered in some cases.

Management of Anxiety

Anxiety in the patient with advanced cancer can be managed as follows:

- *Treat underlying physical problems and discontinue offending medications.*
- *Assess and aggressively manage pain.*
- *Offer reassurance, sensitively address concerns and fears, enable the patient to express his or her thoughts and feelings about the situation, and empower the patient with helpful information.*
- *Suggest relaxation techniques.*
- *Prescribe anxiolytic medications judiciously.*

Antianxiety medications are safe and effective in treating acute and chronic anxiety states in the oncology setting. The choice of an antianxiety medication is usually made based on the severity of the symptoms. For tests, procedures, and episodes of brief anxiety, the shortacting benzodiazepines can be used on an as-needed basis (midazolam, alprazolam, lorazepam). Longer acting benzodiazepines (clonazepam, diazepam) do not wear off as quickly, thereby providing more consistent relief of anxiety symptoms. A relatively nonsedating neuroleptic such as haloperidol or a sedating neuroleptic such as thioridazine may be more effective for a patient who is anxious and confused. Neuroleptics also may be useful for a patient whose anxiety is substance-induced.

Anxiety in patients who are dying is often brought on by one of the many physical complications at the end of life. It is important to remember the psychological causes of anxiety, especially with patients who are alert and not confused. These patients may have fears about disability and dependence. Additionally,The fear associated with death (death anxiety) is a normal part of the human condition. It is the fear of nonbeing, life's ultimate existential concern. In particular, patients may fear the isolation and separation of death and claustrophobic patients may fear the idea of being confined in a coffin. Although these issues are often troubling for staff they should not be avoided. Eliciting assistance from trained spiritual counselors may be an important part of caring for a dying patient.

Supportive counseling is an important intervention for the terminally ill and should be provided by trained professionals. Many fears and concerns of the terminally ill may be too painful to reveal to family and friends. Thus, the goal of supportive counseling at the end of life may be described as helping patients achieve comfort or peace of mind. An open and frank discussion about death and dying may alleviate fears and anxieties by detoxifying or demystifying the experience.

Unique qualities of skilled counselors in this setting include active listening, giving supportive verbal feedback, and eliciting lighthearted conversation about the patient's life and experiences rather than focusing solely on death and dying. This type of counseling requires someone who is adept at stimulating interaction and actively listening with interest rather than somber and emotionally distant.

Palliative Pearls:

- *Factors contributing to anxiety include underlying anxiety disorder, unmanaged pain and medical factors.*
- *Interventions for anxiety may be supportive reassurance, behavioral techniques or pharmacological therapies.*
- *The most important emotion associated with anxiety is fear.*
- *Supportive counseling of the terminally ill may help alleviate fears by detoxifying or demystifying the experience.*

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10 AIDS

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INTRODUCTION

The advent of HIV/AIDS in the world has forced all of us to accept a revolutionary paradigm shift. This paradigm shift is a movement from curing towards caring. There is no cure for AIDS so we have no alternative but to focus our caring on the physical as well as the psychological welfare of the infected individual and his or her significant others.

AIDS has always presented unique medical and psychosocial problems for patients, families and care providers. The stark reality is that AIDS in the developing world presents as a life-threatening illness affecting young adults, often with multiple infected family members, thereby raising difficult issues of premature death, unfinished business, legacy and survivorship. Such an incurable disease is often compounded by guilt, shame, anger and despair, for those infected and affected. In the developing world, the situation is compounded by poverty, unemployment, deprivation, limited resources and increased vulnerability of many patients living with and dying from AIDS.

It is in light of this that primary care providers deliver integrated, comprehensive care over the continuum of illness in ways that combine biomedical and psychosocial approaches within an interdisciplinary model of care. Part of this task involves being familiar and current with the science of Palliative Medicine, just as with the science of HIV medicine. Part of it also involves acceptance of our inability to always defeat death and acknowledgements of our own limitations and vulnerabilities as well as our patient's needs.

The course of HIV/AIDS is different to that of cancer and is far less predictable. The trajectory of HIV/AIDS can be compared to a long and winding road, on a slow decline. All along that road are signposts that, if ignored, will cause patients traveling along that road to fall off the roadside and possibly die. These signposts are the opportunistic infections and cancers that patients may experience.

In Palliative Care it is essential that all reversible and treatable conditions relating to HIV/AIDS are accurately diagnosed and actively treated wherever possible. Palliative Care is not just for patients with advanced late stage HIV disease. Palliative Care is applicable at all stages and includes the active treatment of associated reversible conditions.

EPIDEMIOLOGY

There is a bewildering array of statistics on the past, present and future state of the global AIDS epidemic. They all point to the incontrovertible fact that the epidemic is large and affect every facet of society.

The Global HIV Epidemic

AIDS was first documented over 20 years ago and since then the epidemic has spread throughout the world, but at an uneven pace.

It is estimated that more than 60 million people worldwide have lived with HIV/AIDS since the beginning of the epidemic and 20 million of these have died.

HIV/AIDS now affects every country in the world and in spite of increased knowledge about prevention and treatment, the disease continues to spread.

The HIV Epidemic in Sub Saharan Africa and the Developing World

Globally, Sub Saharan Africa is the most severely affected with 24 million people living with HIV/AIDS in this region, 70% of the global total of HIV+ people.

Southern Africa is the present epicenter of the epidemic, with Botswana having the highest prevalence rate in the world, and South Africa having the highest absolute number (4.8 million) of any country in the world.

HIV epidemics are rapidly emerging throughout Asia. A new explosion of HIV/AIDS is now occurring in Asia, India, China and Russia.

In the developing world, the epidemic is predominantly a heterosexual epidemic transmitted through sexual intercourse, while in Russia, iv drug abuse is also major factor.

TRANSMISSION

HIV can be transmitted from one individual to another through contact with:

- *Blood or blood products*
- *Semen*
- *Vaginal secretions*
- *Breast milk, and*
- *Other body fluids containing blood.*

Most individuals are infected with HIV:

- *Through sexual contact*
- *Before birth or during delivery*
- *During breast-feeding*
- *When sharing contaminated needles and syringes (usually intravenous drug users)*

NATURAL HISTORY

HIV primarily infects and destroys cells in the immune system, particularly CD4 (helper) T-lymphocytes, causing profound immune suppression that gradually develops over a period of years and ultimately renders the patient vulnerable to opportunistic infections (OIs) and malignancy.

In addition to its effects on the immune system HIV also infects nerve, renal, and bone marrow cells with important clinical consequences.

The response to HIV infection varies widely between individuals, ranging from severe seroconversion illness, with rapid progression to immune failure and death, to asymptomatic infection with essentially normal immune function (the 'long-term non-progression').

In the absence of antiretroviral therapy (ART), the median time to AIDS, from the point of infection, is 8-10 years.

There is some evidence that poor socio-economic conditions, including malnutrition and limited access to health care may contribute to a natural history that is one to two years shorter in certain developing countries.

Clinical Staging

The World Health Organization (WHO) staging system for HIV infection allows clinical evaluation of immune function, assessed using standardized criteria. It also takes into account the patient's performance status which is relevant in a Palliative Care setting (Table 1). The Centers for Disease Control and Prevention (CDC) Staging System has not been validated in developing countries and uses CD4 counts as an integral part of staging. This may be difficult to apply in resource-poor settings where access to laboratory facilities is limited.

AIDS – Stage Four

"AIDS" is the term given to the constellation of opportunistic infections and malignancies, as well as manifestations of HIV infection itself (e.g. encephalopathy and the wasting syndrome), that occur when the immune system is profoundly depleted (WHO Stage 4) or when the CD4 cell count drops below 200 cells/µl.

TABLE 1 - The World Health Organization - Clinical Staging System		
WHO Stage 1	Seroconversion illness Asymptomatic infection Persistent generalized Lymphadenopathy Flu-like viral illness	Performance status 1 (fully active and asymptomatic)
WHO Stage 2	Less than 10% weight loss Herpes zoster Minor mucocutaneous manifestations Recurrent upper respiratory tract infections	Performance status 2 (symptomatic but near fully active)
WHO Stage 3	More than 10% weight loss Chronic diarrhea for > 1 month Prolonged fever Oral candida chronic vaginal candidiasis Oral hairy leukoplakia Severe bacterial infections Pulmonary tuberculosis (TB)	Performance status 3 (in bed <50% of normal daytime)
WHO Stage 4 **(AIDS)**	Extrapulmonary TB PCP Cryptococcal meningitis Herpes simplex virus ulcer > 1 month Oesophageal candidiasis Toxoplasmosis Cryptosporidiosis Isosporiasis Cytomegalovirus (CMV) HIV wasting syndrome HIV encephalopathy Kaposi's sarcoma (KS) Progressive multifocal leukoencephalopathy Disseminated mycosis Atypical mycobacteriosis Non-typhoid Salmonella bacteraemia Lymphoma Recurrent pneumonia Invasive cervical carcinoma	Performance status 4 (Confined to bed >50% of normal daytime)

PROGNOSIS

Laboratory parameters determining prognosis

Viral load predicts the rate at which HIV-induced destruction of the immune system takes place, and the CD4 count provides insight into how far the destruction of the immune system has progressed. The CD4 count predicts the risk of opportunistic infections and is used to determine the need for prophylactic therapy and the initiation of ART. Clinical AIDS is defined by a CD4 count of <200 cells/µl

The CD4 count is costly and the total lymphocyte count (TLC) is a less expensive laboratory parameter that provides some prognostic information.

A TLC of <1.25x109/l correlates with a CD4 count of <200 cells/µl

The TLC together, with the WHO Staging System, provides useful prognostic information. An albumin level of <30 g/l is also an indicator of poor prognosis.

Individual prognosis is best determined by integrating a clinical evaluation of the patient's immune status with information provided by the viral load and CD4 count.

Prognostic information can be used to :

- *Give the patient the knowledge to make important personal and social decisions;*
- *Determine when to initiate prophylaxis;*
- *Determine when to initiate ART;*
- *As a guide as to when to continue solely with Palliative Care as disease advances.*

Prognostication in HIV/AIDS is a challenge and clinicians are often unsure of whether to purely palliate or to continue with aggressive interventions.

There are certain guidelines that help determine prognosis further described in this chapter.

ASSESSMENT

The initial assessment of an HIV+ patient should be systematic and comprehensive.

A comprehensive history of a patient with AIDS should include the following:

1. History of HIV Infection

- *Stage of infection;*
- *Presence and chronology of HIV-related illnesses or events; e.g. TB, oral candidiasis, weight loss, rashes, diarrhea;*
- *Use of antiretroviral therapy.*

2. Evaluation of Symptoms (including pain)

- *Frequency*
- *Severity*
- *Quality*

- *Chronology e.g. when did it begin?*
- *Impact on daily activities*
- *Exacerbating or relieving factors*
- *Impact on other symptoms*
- *Impact of therapy on each symptom.*

3. Symptoms review

A Patient with AIDS often has multiple symptoms. A systems review might pick up important symptoms that may have been overlooked.

4. Past Medical History

This aspect reviews all relevant past medical, surgical, STI and psychiatric history.

5. Medication History

Elicit use of

- *prescription and non-prescription medications,*
- *antiretroviral therapies,*
- *alternative herbal and traditional medicines,*
- *complementary therapies,*
- *any drug allergies (especially to cotrimoxazole) and adverse drug reactions.*

6. Family and Social History

This includes:

- *Occupation*
- *Relationships and marital status*
- *Children and support structures*
- *Previous experience with death and dying*
- *Coping skills*
- *Cultural and spiritual issues*
- *Factors preventing full disclosure of HIV status*
- *Questions about life style, (e.g. alcohol and drug use, smoking, diet, exercise and sexual practices and condom use) only if relevant.*

Review of Goals of Care

As with all advanced illness, this is a highly relevant part of the assessment and assists the clinician and care team in defining appropriate treatment strategies.

The patient's priorities may be very different from the clinicians. Set realistic goals and objectives with the patient and then operate within that framework.

Physical Examination

This aspect of the assessment is important for establishing the etiology of each symptom.
In advanced HIV disease, multiple symptoms may be present and so a full clinical examination is usually appropriate, with attention to neurological and mental state examinations.

Investigations

In a Palliative Care setting, Radiological investigations and laboratory tests such as CD4 count, viral load, full blood count, total lymphocyte count, syphilis serology, sputum smears, urea, electrolytes and glucose, should be taken only where appropriate; e.g. in defining the etiology of a symptom. The degree of investigation depends on the stage and clinical condition of the patient as well as on the patient's goals and aspirations.

Problem List and Treatment Plan

1. *Draw up a problem list.*
2. *Define the etiology of the symptom with the aim of treating the cause where possible. Often the best palliation is achieved by treating the primary cause of the symptom.*
3. *Develop a strategy that is aimed at relieving the distress associated with the symptom. At the end of life it is often not possible to treat the cause and quality of life is the important outcome of all treatments.*
4. *Draw up the treatment plan.*
5. *Regularly evaluate the impact of the treatment plan.*

Monitoring

A follow up plan should be made for reassessment and monitoring.

MANAGEMENT

Primary Prophylaxis and Immunisation

Most of the morbidity / mortality in patients with AIDS result from opportunistic infections. Primary prophylaxis and/or immunization can prevent many of these infections from occurring. Good Palliative Care includes prevention of infections through primary prophylaxis and prevention of recurrence, through secondary prophylaxis.

Co-trimoxazole Prophylaxis

Co-trimoxazole provides protection against Pneumocystis carinii pneumonia, Toxoplasmosis, many bacterial infections and diarrhea caused by Isospora Belli or Cyclospora species.

Prophylaxis with Co-trimoxazole is indicated in all HIV-infected individuals who are immunosupressed; a CD4 count of <200 cells /µl or total lymphocyte count of <1.25 x 109/l or WHO Stage 3 or 4.

The standard dose is 960mg daily but lower doses (480mg daily) are probably as effective.

HIV AND TB (Tuberculosis) (See Chapter 11)

The AIDS epidemic has caused a parallel rise in the TB epidemic and has changed the epidemiology and natural history of tuberculosis (TB) in many parts of the world. HIV infection is the strongest risk factor for the progression of latent Mycobacterium tuberculosis infection to active TB. Immune deficiency also causes reduced resistance to newly acquired TB. TB is the most common life-threatening HIV-related infection worldwide and is often the sentinel illness of HIV infection. To date, well in excess of 15 million people are estimated to be co-infected with HIV and TB. (See Chapter 14)

In most countries in Sub Saharan Africa more than 50% of patients with TB will test positive for HIV. Up to 80% of patients admitted in TB hospitals, who are too ill for ambulant care, are young adults with HIV co-infection.

The increased risk of TB in untreated HIV infection is a result of the progressive immunosuppression that predominantly affects cell-mediated immunity. However, there is emerging evidence that TB accelerates HIV disease, with a more rapid progression to acquired immune deficiency syndrome (AIDS) and death. This accelerated HIV disease progression is thought to be induced by immune stimulation.

Isoniazid (INH) at a dose of 300mg daily, given for 6 months, is the best- studied regimen in HIV infection. Combined tablets of Rifampicin with either INH for 3 months, or Pyrazinamide for 2 months are also effective.

It is essential to exclude active TB prior to commencement of TB preventive therapy.

TB prophylaxis is indicated for:

- *Individuals with TB contacts*
- *Miners and prisoners*
- *Patients with tuberculin skin test of >5mm*
- *Malaria Prophylaxis (See Chapter 13)*

There are no significant interactions of medications used to prevent malaria, including mefloquine, and antiretroviral therapy. HIV-infected individuals can safely take malaria prophylaxis.

Immunization

Pneumococcal Vaccine has currently not shown to be effective in the developing world in patients not on antiretroviral therapy.

Influenza Vaccine is recommended annually if CD4 count over 200 cells/µl. Patients with HIV disease can safely be given inactivated vaccines including Hepatitis A and B. Yellow Fever vaccine is contraindicated in patients with WHO Stage 3 or 4 disease with a CD4 count of < 200 cells/µ

ADULT ANTIRETROVIRAL THERAPY (ART)

Without access to ART, AIDS can be a rapidly fatal acute infectious disease characterized by multiple opportunistic infections, rapid deterioration and death. The impact of ART on the natural history of HIV infection results in a much more variable trajectory of illness, more typical of a chronic progressive illness. However, the advent of ART has not diminished the need for Palliative Care for people living with HIV/AIDS.

In the developing world the benefits of ART are not always attainable due to lack of financial resources and access to the drugs. Poverty and lack of basic nutrition make it difficult to adhere to strict treatment regimens which results in progressive viral resistance.

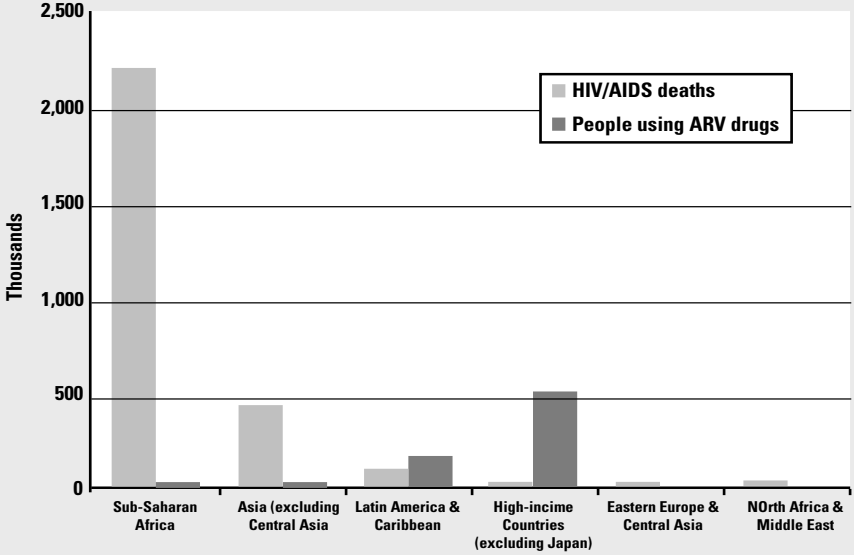
For all these reasons, comprehensive AIDS care in the developing world must continue to encompass Palliative Care throughout the continuum of illness. Even if patients have access to ART, palliative and curative approaches must be incorporated in all stages of illness. ART is, at times, responsible for additional symptoms, (e.g. painful neuropathy and gastrointestinal disturbances) which can also be relieved by effective Palliative Care.

An overly narrow focus on ART and the technical biomedical details of HIV care will neither do justice to the patient's condition, nor ultimately promote a meaningful patient/physician relationship.

The cost of ART is falling rapidly and is becoming progressively more available in the developing world. Often the most effective Palliative Care for a patient with HIV/AIDS is ART. Palliative Care clinicians should therefore have a basic knowledge of the available antiretroviral medications and their uses.

When the current number of HIV/AIDS-attributable deaths is contrasted with the number of people using ART in different regions of the world, the current global inequality in the treatment is startling as seen in Figure 1.

HIV/AIDS deaths in 2001 and number of people using antiretroviral drugs by region



Improvement in mortality and morbidity due to availability of ART is notable in Brazil and should become visible during the next few years in Latin America, the Caribbean and Asia.

Generic drug manufacturers in countries such as Thailand, India and Brazil, are producing their own versions of certain antiretrovirals for use in their domestic, and in some cases, overseas markets.

Many countries (e.g. Botswana, Barbados, Benin, Burkina Faso, Burundi, Chad, Cameroon, Chile, Republic of Congo, DRC, Côte d'Ivoire, Gabon, Honduras, Jamaica, Malawi, Mali, Morocco, Romania, Rwanda, Senegal, Trinidad, Tobago and Uganda) have reached agreements with manufacturers on significantly reduced drug prices.

Despite these advances, of the 28.5 million total number of people living with HIV/AIDS in Sub Saharan Africa, fewer than 30 000 people had benefited from ART at the end of 2001. In Asia and the Pacific, of the estimated 6.6 million people living with HIV/AIDS at the end of 2001, less than 30 000 had access to ART. In Latin America and the Caribbean, it is estimated that 170 000 people of approximately 2 million living with HIV/AIDS, were receiving ART at the end of 2001.

ART stops the progression of HIV disease and reduces the HIV viral load in the blood. This allows some recovery of the immune system and a reduction of HIV-related diseases. ART is complex, requiring the use of at least 3 drugs in combination and a patient may be required to strictly adhere to taking many tablets for many years.

Non-adherence results in viral resistance to the tablets. More than 95% of the tablets must be taken to maintain viral suppression. It is now generally accepted that patients should not commence therapy too early in the course of infection, but should start when CD4 count is <200 cells/µl or the patient shows severe symptoms of HIV disease; (Stage 3 or 4 WHO Staging System). Ideally ART should start before the CD4 count drops below 50 cells/µl. Treatment is more successful and better tolerated for patients with less advanced disease. Patients need to be educated about the therapy, possible side effects and results of non-adherence. They need to be committed to potential life-long therapy.

There are 3 classes of antiretroviral medications available:
- *Nucleoside reverse transcriptase inhibitors (NRTI)*
- *Non-nucleoside reverse transcriptase inhibitors (NNRTI)*
- *Protease inhibitors (PI)*

A triple therapy combination will use either 3 NRTIs or 2 NRTIs with either a NNRTI or a PI.

Health Care Professionals will need to be aware of which antiretrovirals are currently registered in their country.

PALLIATIVE MANAGEMENT

This chapter focuses on the Palliative management of symptoms related to AIDS, rather than on the specific opportunistic infections and disease which occur in HIV/AIDS.

Constitutional Symptoms

Constitutional symptoms such as weight loss, fatigue, fever and sweats are very common in patients with advanced HIV/AIDS. Attempts to treat the underlying cause should be made, however in many cases the underlying cause is refractory to treatment.

Anorexia and Wasting

Wasting in HIV/AIDS is caused by many different mechanisms including the uncontrolled inflammatory state, inadequate nutrition, excessive nutrient loss and a metabolic dysregulation with abnormal protein catabolism and over secretion of cytokines. Other factors that contribute to anorexia and wasting include: odynophagia and dysphagia from candidiasis, herpes and apthous ulcers, nausea, side effects of medication, pain, depression, anxiety, malabsorption, chronic TB, hypogonadism and alterations in cortisol metabolism.

The palliative management of anorexia includes the following options:

General Measures:

- *maintain good oral hygiene. Keep the mouth fresh with a mouthwash of 1 teaspoon salt, vinegar or lemon juice in 1 liter water.*
- *Keep the mouth moist with lubricating jelly, e.g. KY jelly and the lips lubricated with petroleum jelly*
- *keep meals small and frequent – avoid food with strong odors*
- *encourage oral fluids*
- *a small amount of alcohol before meals may stimulate appetite*

Pharmacological Measures

Appetite stimulants:

- *Megestrol acetate (also shown to cause weight gain): 80-160 mg bd*
- *Corticosteroids: e.g. dexamethasone: 2-4 mg daily or prednisone: 10-20 mg daily*
- *Periactin (may also stimulate the appetite) 4 mg bd or tds*

Antiemetics:

- *metoclopromide for nausea of gastrointestinal origin: 10-20 mg tds (if nausea contributes to the anorexia)*
- *haloperidol for drug-induced nausea 1-2.5 mg nocté*
- *cyclizine with (dexamethasone) for nausea related to raised intracranial pressure: 50 mg tds*

Symptoms of thirst and hunger are reduced or absent in patients with advanced AIDS and caregivers should not "force feed" patients, which leads to frustration and guilt. Artificial feeding will not prolong life nor improve quality of life.

Weakness and Fatigue

HIV/AIDS related fatigue and weakness are common and usually multi-factorial in origin. Fatigue and weakness severely compromise quality of life.

Reversible conditions such as infections, vitamin deficiencies (e.g. iron, B12 and folate), anemia and depression should be treated where possible. However conditions relating to HIV disease progression, metabolic abnormalities, malignancy and end stage organ failure are usually irreversible.

The palliative management of weakness and fatigue include the following:

General Measures

- *Planning and pacing activities*
- *Promoting adequate sleep and rest*
- *Adequate nutritional and vitamin supplementation (however as the patient's disease advances less pressure should be placed on the patient to eat more than they are able)*
- *Caregivers should assist with daily activities of living, ensuring a safe environment and supervision when a patient is in danger of falling.*

Pharmacological Management of Weakness and Fatigue
Cortico steroids (temporarily improve fatigue)
dexamethasone 2-6 mg / day
**Psychostimulants*
Methylphenidate 2.5-5mg at 08h00 or 2.5-5 mg bd at 08h00 + noon
The dose can be gradually increased to a maximum daily dose of 60 mg.
**Dextroamphetamine and pemoline have been used in the USA in patients with advanced HIV disease; however they are not always available in developing countries.*

Fever and Sweats

Fever is caused by infections (e.g. TB), HIV associated malignancies, drug side effects (eg. Trimethoprim-sulfamethoxazole), hormonal dysfunction and autoimmune disorders. Fever can be caused by HIV itself. Sweating without fever can occur with certain infections, malignancies, endocrinopathies and medications (e.g. opioids). Different options in the palliative management of fever include:

General Measures:

- *Promote heat loss through loose clothing and sheeting or loosely-woven blanket;*
- *Regular changes of linen and clothing;*
- *Keep pillow dry with a frequently changed cloth or towel covering;*
- *Emollient creams for dry skin;*
- *Maintain fluid and nutritional intake.*

Pharmacological Management of Fever and Sweating

Antipyretics:

Paracetamol 500-1000 mg 6 hrly (Use regularly around the clock)

Ibuprofen (NSAID) 400 mg tds

Corticosteroids:

dexamethasone 2-6 mg / day

*Anticholinergics:

scopolamine adhesive 1.5 mg patch

hyoscine butylbromide 20 mg orally tds or subcutaneously

H2 antagonist:

cimetidine 400-800 mg po bd

** Other anticholinergics such as glycopyrrolate are often not available in the developing world*

Gastrointestinal Symptoms

Gastrointestinal symptoms are ubiquitous in patients with AIDS.

Dry Mouth

Although there are numerous conditions contributing to a sore dry mouth, such as candidiasis, apthous ulcers and herpes simplex, a dry mouth is often simply caused by mouth breathing. Other causes include drugs such as antiretrovirals, anti-histamines, anti-convulsants, anti-depressants and anti-cholinergic drugs which reduce salivary flow. The HIV infection itself can also cause xerostomia. Dehydration, reduced mastication, anxiety and depression all reduce salivary flow. Oxygen therapy aggravates a dry mouth.

There is no evidence that rehydration results in any relief of xerostomia and simple p alliative measures are usually more than adequate.

The Palliative Management of Xerostomia

- *good oral and dental hygiene*
- *treatment of infections such as candidiasis, herpes simplex*
- *review drug regimen – reduce dosage or change the drug if possible*
- *artificial saliva products are costly and often not available in the developing world. "Home made" saliva (methylcellulose + lemon essence + water is a possibility, but methylcellulose is often unavailable in the developing world.)*
- *in patients with advanced disease, lubricating jelly (KY jelly) applied to tongue and oral cavity has been shown anecdotally to be an affordable and effective means of keeping the oral cavity moist and lubricated.*
- *Lip moisturizers, e.g. petroleum jelly or flavored lip gels*
- *Frequent sips of cold water. If patient is very ill, spray cold water into mouth using a spray bottle or use a sponge stick*
- *Offer a mouthwash 2-hourly e.g. saline sodium bicarbonate solution; a chlorhexidine solution; or a homemade mouthwash of 1tsp of salt, vinegar or lemon juice in one liter of water.*
- *during eating, lubricate the inside of the mouth with a little butter, margarine or salad oil*

- *humidify the room in areas where the air is very dry*
- *suck ice cubes, vitamin C tablets, sugar-free lemon flavored sweets, sour sweets.*
- *chew sugar-free gum.*
- *chew or suck fresh pineapple chunks*

Oral Candidiasis

Virtually all patients referred to Palliative Care services have oral or esophageal candidiasis at some stage.

Anecdotal evidence suggests that simple and inexpensive measures are often effective and include:

- *Chlorhexidine digluconate mouthwash*
- *Povidone-iodine ("Betadine") mouthwash*

It is important that these mouthwashes are used regularly after every meal and 3-4 hourly if possible. Chlorhexidine used long term can stain the teeth.

Other options include:

- *Nystatin suspension 100 000 µg/ml (2.5ml 5 times daily)*
- *0.5% gentian violet aqueous solution painted in the mouth 3 times daily.*
- *2% Miconazole gel applied 2-3 times daily*
- *Amphotericin B lozenges 10mg 6 hourly*
- *Systemic treatment with azole medication, e.g.*
  Ketoconazole: 200-400mg daily
  Fluconazole: 50-100mg daily
  Itraconazole: 200mg daily

Although oral azole medications are very effective, they are expensive and may not be available to patients in the developing world. However, azole medication is the treatment of choice for esophageal candidiasis.

Apthous Ulceration

- *Control pain with :*
  1. *oral analgesia (WHO analgesic ladder)*
  2. *Topical analgesia e.g. 2% Lignocaine gel; Benzydamine mouthwash; Benzocaine spray; Morphine mouthwash : 15mg ampoule of Morphine sulphate added to saline or Benzydamine mouthwash, not swallowed (anecdotal)*
- *Topical steroids, e.g. Triamcinolone paste (Kenalogg in Orabase) Beclomethasone spray (1-2 puffs twice daily onto ulcer); Betametasone 0.5mg tablets dissolved in 15ml water used as a mouth wash for 3 minutes (not to be swallowed)*
- *Chlorhexidine digluconate mouth washes 2-4 times daily.*
- *Systemic steroids may be used for long-standing intractable ulcers, e.g. Prednisolone. (It is important to exclude CMV and herpes ulceration before using steroids, as steroids exacerbate these ulcers.)*

- *Thalidomide (50-100mg nocté) is a useful alternative to steroids, but may aggravate pre-existing peripheral neuropathy.*
- *Tetracycline mouth wash and gargle: empty the contents of a 250 mg capsule into ± 50 ml water or saline tds, not necessary to be swallowed. (Anecdotal)*

Diarrhea

Diarrhea is the most common gastro-intestinal symptom in HIV/AIDS. Diarrhea is most commonly caused by infection, but drugs (some antiretrovirals and antibiotics) may be responsible. Malignancies and mal-absorption may also present with diarrhea. The cause should be identified and treated, although this is often not possible in a patient with advanced disease. In advanced disease, even if a specific pathogen is isolated, the availability of treatment is limited and the response disappointing. However, it is essential that clinicians and patients be aware that if a patient with a history of chronic diarrhea presents with an acute episode with fever, cramping and per rectal bleeding, they should be actively investigated. It should not be assumed to be untreatable and simply accepted as part of the disease process. A lack of response or a late response could cause a patient to die unnecessarily.

Pathogens responsible for Diarrhea in HIV Disease:

- *Protozoa (Cryptosporidium, Giardia lamblia, Entamoeba histolytica, Isospora belli)*
- *Bacteria (Salmonella, Shigella, Campylobacter)*
- *Viruses (Cytomegalovirus, Herpes Simplex, HIV itself)*
- *Mycobacterium avium intracellulare and microsporidia*
- *Cryptosporidium is the most common pathogen and a major cause of morbidity with intractable watery diarrhea associated with mal-absorption, profound weight loss and malnutrition.*

Symptomatic management is often the only feasible treatment and aims at:

- *reducing the number and frequency of stools*
- *thickening the consistency*
- *reducing colicky abdominal pain that is often associated with diarrhea.*

Symptomatic treatment should not be delayed until the patient has been fully investigated or until failure of specific therapy has been demonstrated

General Measures:

- *A bowel chart kept by the patient or carer is a useful tool*
- *Rehydration orally, intravenously or subcutaneously (hypodermoclysis) may be necessary especially if the diarrhea is of acute onset with rapid development of dehydration*
- *Avoid spicy, high fiber and greasy foods that could exacerbate diarrhea. Dilute fruit juices. Avoid caffeine and alcohol; extremely hot or cold foods*
- *high-energy low-residue soft foods (e.g. maize meal, bananas, rice, white bread, peeled potatoes and grated apple)*
- *Avoid drugs that increase peristalsis, such as metoclopramide and domperidone*
- *Exclude faecal impaction and spurious diarrhea which could occur in patients on opioid and other constipating drugs*

- *Apply a protective petroleum-based (Vaseline) ointment to the perirectal skin to prevent excoriation. Keep perirectal area clean and dry.*

Oral antidiarrheal agents:
Loperamide: (drug of first choice) 4mg stat, 2mg after each loose stool up to 32mg over 24 hrs.
Codeine phosphate: (a less costly alternative to Loperamide) 30-120 mg 4-6 hourly
*Morphine elixir: an alternative to *Codeine from 5 mg 4 hourly titrated upwards*
Hyoscine butylbromide : (an antispasmodic which may reduce bowel activity and colic) 20 mg tds
Bulking agents e.g. ispaghula husk or psyllium to thicken the stool
Cholestyramine for patients with secondary malabsorption
Kaolin-pectin preparations

**Some clinicians avoid combinations of Morphine, Codeine and Loperamide, as they all have the same mechanism of action via opioid receptors in the intestinal tract. However, Codeine or Morphine have been prescribed in combination if Loperamide alone is ineffective.*

- *In some patients a brief empiric trial of an anti-infective agent such as metronidazole, quinolones, tetracyclines or sulphonamides may be initiated. Therapy with gancilovir for CMV colitis is usually unavailable in resource-poor setting. Consider Albendazole for microsporidia infection.*

Symptomatic control of diarrhea is important not only for improving patient comfort, but to facilitate the absorption of active treatment given orally.

Parenteral Management

- *For severe intractable diarrhea with or without nausea and vomiting, medication can be given subcutaneously, ideally with the use of a syringe driver. For the control of severe diarrhea and/or vomiting, prescribe a continuous subcutaneous infusion of:*
  1) *antidiarrheal agent (morphine sulphate)*
  2) *anti-emetic (cyclizine and/or haloperidol)*
  3) *antispasmodic/antisecretory agent (hyoscine butylbromide or octeotide)*
- *octreotide is a synthetic somatostatin analogue that is useful in patients with profuse watery diarrhea. It is very costly and is administered subcutaneously and may not be available for use in the developing world.*

Constipation

Constipation can cause severe colicky pain, nausea and even vomiting. In the developing world constipation is not a common problem in patients with AIDS.

However, in patients on antiretroviral therapy or on anti-diarrheal or opioid therapy, clinicians need to be aware of the potential for developing constipation.

Patients with advanced disease usually prefer a low residue, low fiber diet, have a limited fluid intake and reduced physical activity and are therefore at risk of becoming constipated.

- *preventative action to avoid constipation is the most effective management*
- *encourage fluid intake and mobilization and increase dietary fiber (if appropriate)*
- *Laxative therapy*

Laxative Therapy

Stimulant laxatives: bisacodyl (Ducolax), sennakot
Emollient/lubricating laxatives: liquid paraffin
Osmotic laxatives: lactulose
Saline laxatives: magnesium hydroxide (milk of magnesia)
**Suppositories or enemas: glycerine or bisacodyl (Ducolax)*
** Suppositories or enemas may be given if oral laxatives alone are insufficient*

Because of the high incidence of diarrhea in patients with advanced AIDS in the developing world, caution should be exercised when using laxatives in this population. It may be appropriate to start with low doses of the lubricating or osmotic laxatives before attempting stimulant laxatives.

A combination of magnesium hydroxide (milk of magnesia) and liquid paraffin in a ratio of 3:1 is an inexpensive and effective laxative, ideal for use in the developing world. Dose: 10-20 ml once daily - tds.

Nausea and Vomit

- *almost all patients with AIDS experience nausea and vomiting at some stage*
- *for some it is extremely resistant to treatment*

Possible causes of Nausea and Vomiting in Patients with Advanced AIDS:
** poor oral hygiene*
** drugs, eg ddi, pentamidine, opioids*
** oropharyngeal candidiasis*
** infections and fever*
** esophageal herpes*
** cerebral tumors*
** diarrhea*
** cerebral abscesses and infections*
** constipation*
** raised intracranial pressure*
** gastric irritation*
** fear, anxiety*
** infections of liver and gall bladder*
** uremia*

Palliative Management of Nausea and Vomiting in a Patient with AIDS

General Measures:

- *Assess and manage dehydration*
- *Elevate the patient's head after meals*

- *Keep meals small and frequent*
- *Avoid fried, fatty and strong smelling foods*
- *Minimize the smell and sight of cooking*

Pharmacological Therapy:

- *The Palliative Management of nausea and vomiting often requires a combination of different anti-emetics working at different levels.*

Anti-emetics need to be given on a regular schedule so that the patient does not re experience the problem. Determination of the cause or site of nausea and vomiting guides the use of anti-emetics

Oral Antiemetics:

1st Line Oral Antiemetics

*Metoclopramide: *Start with 10—20mg tds, increase to 60-120 mg / 24 hrs if necessary*
Cyclizine: 50mg tds
Haloperidol: 1-5mg daily

2nd Line Oral antiemetics

Hyoscine butylbromide: 20mg tds
Dexamethasone: 2-4 mg daily
Prochlorperazine: 5-10mg tds
**Use higher doses with caution in patients with AIDS due to CNS toxicity.*

Parenteral Antiemetics

Oral medication is the preferred route; however, severe vomiting requires antiemetics given via a parenteral route. The ideal method is a continuous subcutaneous infusion via a portable battery-operated syringe driver (e.g. Graseby)

Antiemetics Administered Subcutaneously:

Cyclizine: 50-100mg/24 hours
Hyoscine butylbromide: 20-120mg/24 hours
**Other Options:*
Dexamethasone: 2-4mg/24 hours
Octreotide: 150-300µg/24 hours
Ondansetron: 4-8mg/24 hours

**These are expensive and may not be readily available in developing countries. Dexamethasone does not mix well with other drugs used in a syringe driver and needs to be given separately.*

- *In areas where there is no access to a syringe driver, the antiemetics can be given subcutaneously as stat doses 2 – 3 times a day. The insertion of a "butterfly" needle subcutaneously on the anterior chest wall provides a port for repeated injections. The site can be changed every 3-4 days or as needed.*
- *Rectal suppositories are another alternative in patients who do not have concomitant diarrhea or anorectal disease.*
- *Extrapyramidal side effects are more likely in patients with AIDS.*

Dermatological Symptoms

Malodorous Wounds

This is a most distressing symptom which is unfortunately common in patients with advanced HIV disease, living in resource-poor settings. The odor is often caused by contamination by anaerobic bacteria.

Examples of Malodorous Wounds

- *– perianal abscesses, ulcers and excoriation*
- *– vaginal infections*
- *– bed sores*
- *– perineal infections*
- *– fungating tumours*
- *– carcinoma of the cervix*
- *– oral lesions*

Management Options

- *Regular cleansing with "Flagyl Solution" : 2 liters saline + 13 (400mg) crushed Metronidazole tablets*
- *"Flagyl Gel" : KY jelly or Intrasite (desloughing) gel mixed with crushed Metronidazole tablets applied topically to wound*
- *"Flagyl Cream" : 1 large tub (500ml) of UEA Cream mixed with 20 (400mg) Metronidazole tablets applied topically to wound*
- *"Flagyl Powder": Crushed Metronidazole tablets sprinkled over wound when a dry dressing is preferred.*
- *For severe cases: oral Metronidazole 400mg bd for as long as necessary.*
- *Other options: charcoal dressings, live yoghurt or honey.*

Dry Skin and Pruritis

Pruritis or itching is the most common dermatological symptom experienced by patients with HIV/AIDS and can be so severe as to cause suicidal thoughts.

Often in advanced stages of AIDS, patients suffer from itching caused by a combination of multiple pathologies such as xerosis cutis, scabies, folliculitis, obstructive biliary disease, adverse drug reactions, renal and liver failure, anxiety and depression.

Generalized Xerosis Cutis

Generalized dry skin with flaking, itching, cracking and fissuring makes skin vulnerable to secondary infection.

Dry skin is found in almost all patients with advanced disease but is particularly severe in patients who have suffered a slowly progressive debilitating process with persistent diarrhea and weight loss.

Management

The goal of management is to break the itching/scratching cycle.

The most effective way to mange pruritis is by preventing and managing the dry skin.

General Measures:

- *Treat any underlying pathological process, e.g. scabies, folliculitis, dermatitis*
- *Use soap sparingly, if at all*
- *Substitute soap with UEA cream (Ung Emulsificans Aqueous)*
- *Do not bath/shower more than once a day and avoid hot water*
- *Use soft non-abrasive sponges, wash-cloths and towels*
- *Moisturize frequently 2-4 times a day with UEA cream, body lotions or lanolin*
- *Add soluble bath oil or 1 tablespoon of UEA cream to bath water*
- *Avoid electric blankets*
- *Avoid sitting near a fire or heater*

Topical Agents to Manage Dry Skin and Pruritis:

- *UEA with 1% menthol*
- *"Eurax" cream (Crotamiton) is a scabicide with anti-pruritic properties*
- *Calamine lotion*
- *Hydrocortisone 1% cream*
- *Hydrocortisone in menthol 1:3*
- *Antihistamine cream*
- *Phenol 0.25%*

Oral Agents to Manage Dry Skin and Pruritis

**Antihistamines*

Diphenhydramine: 50mg tds

Chlorpheniramine: 4-12 mg daily

Hydroxyzine: 15-20mg 8-12 hourly or nocté

Promethazine: 10-25mg nocté

Corticosteroids

Prednisolone: from 5 mg daily

H2 receptor antagonists:

Cimetidine: 400 mg daily

Non-steroidal anti inflammatory drugs

Ibuprofen: 400 mg tds

Cholestyramine

Thalidomide: 50-100 mg nocté

** These are sedating and are usually only administered at night. Non-sedating antihistamines are more expensive and less available to most patients in the developing world.*

Respiratory Symptoms

Cough and Dyspnea

Possible causes of coughing and dyspnea in a patient with AIDS:

- *Pulmonary infections, e.g: Pneumocystis Carinii Pneumonia*
  Pulmonary TB
  Cryptococcal Pneumonia
  Streptococcal Pneumonia
  Haemophilis Influenza Pneumonia
- *Increased respiratory secretions*
- *Chronic bronchitis and bronchiectasis*
- *Bronchospasm (COPD, asthma)*
- *Tumors of the lung, e.g. Kaposi's Sarcoma, Non-Hodgkins Lymphoma*
- *Aspiration*
- *Sinusitis and post nasal drip*
- *Esophageal reflux*
- *Lymphocytic Intersititial Penumonitis (usually in children)*
- *Spontaneous pneumothorax (usually caused by PCP)*

Management of Cough

Cough from bronchospasm:
Often responds to brochodilators: (e.g. inhaled salbutamol) and/or inhaled or systemic corticosteroids
Cough from esophageal reflux:
Warrants a trial of H2 receptor antagonists e.g. Ranitidine or proton pump inhibitors
Dry, irritating non-productive cough: Cough suppressant
e.g: Codeine: from 10-20mg q4h
Dextromethorphan from 25mg tds
Morphine - start with 2.5mg q4h
Demulcents
e.g: simple linctus
**Nebulised lignocaine/lidocaine: -3ml of a 2% solution (without epinephrine) 3-4 times a day*

Productive cough in patient who is able to cough effectively
Nebulised 2.5% saline
Physiotherapy
A mucolytic may be of some benefit in loosening tenacious secretions e.g. Acetylcysteine
Mesna
Bromhexine
Humidification
Productive cough in a patient who is too weak to cough effectively
Codeine: 10-20 mg 4 hourly
Morphine: from 2.5mg 4 hourly
Dextromethorphan 25-50mg tds-qid

** This causes decreased sensitivity of the gag reflex and patients should avoid drinking or eating for an hour after nebulisation. Use Lignocaine with caution in asthmatics as there is a risk of bronchospasm.*

Dyspnea

Dyspnea can also be caused or exacerbated by:

- *anxiety and fear*
- *generalized weakness*
- *anemia*

Non Pharmacological Management of Dyspnea

- *Oxygen if hypoxic. Home oxygen is often not available in resource-poor settings and once a patient has started oxygen, it is very difficult to stop due to psychological dependence, therefore use with caution*
- *A cool stream of air in the face is often as effective as oxygen via a mask*
- *Positioning should be determined by patient preference. The patient's head should be elevated and when one lung is obstructed, lying on one side or the other may help*
- *Relaxation techniques and distraction*
- *Reassurance, explanation and company*
- *Breathing re-training*
- *Physiotherapy*

Pharmacological Management of Dyspnea

A combination of an opioid and a sedative anxiolytic is very effective.

Opioids:

If opioid-naïve, start with 2.5mg – 5mg oral Morphine solution 4 hourly. If necessary, titrate the dose upwards. Morphine improves the quality of breathing and decreases anxiety.

In a patient who is unable to swallow, opioids can be given subcutaneously, sublingually or rectally (Morphine slow-release tablets can be used rectally)

Anxiolytics:
Lorazepam (0.5-1mg po or sublingual 6-8 hourly)
Diazepam (2.5mg tds, then 5mg daily)
Midazolam (from 15mg / 24 hours by continuous subcutaneous infusion) is the parenteral Benzodiazepine of choice.

Other management options depend on etiology:
Corticosterioids
Hyoscine Butylbromide
Bronchodilators

Pulmonary Secretions

As a patient becomes weaker and more exhausted, coughing becomes more difficult and less effective.

Saliva and secretions associated with pulmonary infections or chronic bronchitis build up and pool in the mouth, pharynx, larynx, trachea and main bronchus. This causes a condition sometimes termed "the Death Rattle" which is very distressing for carers and loved ones, but may not always be as distressing for the patient.

Management of Increased Secretions

In the terminal stages in AIDS patients who are too weak to cough effectively, secretions should be reduced by antisecretory (anticholinergic) drugs. To achieve optimal effect, these should be started earlier rather than later.

Pharmacological Management

Hyoscine butylbromide: 20-120mg orally in divided doses or by continuous subcutaneous infusion
Scopolamine transdermal patches: 1.5mg patch; 1-3 patches applied every 72 hours
Antihistamines e.g. Diphenydramine 25-50mg 4-6 hourly

General measures:

- *Frequent re-positioning (avoid supine position)*
- *Position semi-prone to encourage postural drainage*
- *Explanation and reassurance for Care Givers*
- *Reserve suctioning for unconscious patients or for suctioning of oral cavity only.*

PSYCHIATRIC SYMPTOMS

HIV is a neurotropic virus that invades the central and peripheral nervous systems and causes frequent neurological complications. However, changes in mental status are always to be considered abnormal, not simply accepted as an understandable problem.

Delirium

Delirium is common in patients with advanced AIDS and may be caused by many different conditions. In over 50% of cases, the cause is not identified.

Possible Causes of Delirium in AIDS:

- *Central Nervous System infection with or without fever, e.g: viral meningitis, HIV encephalitis, herpes encephalitis, CMV encephalitis, cryptococcal meningitis, TB meningitis, toxoplasmosis, neurosyphilis*
- *Opportunistic infection of the respiratory and gastrointestinal and urogenital tract*
- *Central Nervous System tumours (e.g: lymphoma and Kaposi's sarcoma), seizures, post seizure stages or abscesses*
- *Drugs, e.g. antiretrovirals, opioids, anticholinergics, antibiotics, corticosteroids*
- *Drug withdrawal*
- *Traditional/herbal remedies*
- *Metabolic disturbances*
- *Anemia*
- *Vitamin deficiency*
- *Pruritis*

- *Hypoxia, e.g. due to pneumonia*
- *Anxiety and depression*

Delirium may be precipitated or aggravated by:
- *Excess cold / heat / stimuli*
- *Full bladder or rectum*
- *Pain*
- *Pruritis*
- *Dehydration*
- *Anxiety and depression*
- *Fatigue*

Treatment of Delirium
- *Treat underlying etiology if possible. Always rule out and treat any acute process. Blood tests to detect metabolic changes, urinanalysis, lumbar puncture or CT scan may be required.*

Non-Pharmacological Measures
- *Provide a safe, uncluttered environment*
- *Ensure continuity of care*
- *Place mattress on floor if necessary*
- *Orientation of patient (clock, calendar, explanation)*
- *Night light*

Pharmacological Measures
- *Proceed with caution with drugs and monitor carefully as patients with AIDS have increased sensitivity to drugs that affect the Central Nervous System. All patients with delirium should be treated initially with Haloperidol and other anti-psychotic drugs. Benzodiazepines should only be used if other measures fail.*
- *Haloperidol (from 2.5mg po daily, increase as needed)*
- *Chlorpromazine (from 10—50mg tds)*
- *Risperidone (0.5-1mg bd)*

For severe agitation at the end-of-life:
- *Midazolam:15-60mg / 24 hrs via continuous subcutaneous infusion or*

2.5-5mg stat subcutaneously or po (repeat as needed)
- *Haloperidol: 5-10mg subcutaneously or IV repeat after every 30 min until patient calms or 5-40mg continuous subcutaneous infusion*
- *Benzodiazepines*

e.g. Diazepam 2.5-5mg po tds, then 5-10 po mg nocté
Lorazepam 0.5-1mg sublingually tds

HIV Associated Dementia (AIDS Encephalopathy)

AIDS encephalopathy is a common neurological complication of AIDS and has a high prevalence in

countries with reduced access to ART.

It is due to the direct effect of HIV on micrological cells in the Central Nervous System and has an insidious onset and a chronic course.

AIDS encephalopathy presents with a triad of varying degrees of:
- *Motor dysfunction*
- *Cognitive dysfunction*
- *Behavioral dysfunction*

Signs and symptoms of motor dysfunction include clumsiness, ataxia, tremor, weakness, incontinence, myoclonus and paraparesis.

Cognitive dysfunction ranges from impaired concentration and judgment, poor short-term memory, disorientation, to confusion, hallucinations and psychosis.

Behavioral changes range from loss of interest, withdrawal or reduced inhibition, poor self-care, labile mood, to paranoia and personality changes.

Non-Pharmacological Management
- *The Palliative Management of a patient with dementia includes provision of support, guidance and counseling for the Care Givers.*
- *Supportive and cognitive behavioral therapy;*
- *Environmental management is essential and includes orientation, consistency and limit setting.*

Pharmacological Management

If the patient is anxious and restless consider the following options:
- *Benzodiazepines: eg: Diazepam: start with 2.5-5mg tds. later 5-10 mg nocté*
- *Haloperidol: 1-5mg daily or td.s*
- *Thioridazine: from 10mg daily*
- *Chlorpromazine: 10-25mg tds*
- *Risperidone* start with 0.5-2mg daily and increase slowly to 6mg daily*
- *Olanzapine * 2,5-10mg daily*

If there is psychomotor slowing and reduced attention, consider the following options :
- *Dextroamphetamine: 5-60mg per day, 4-6 hourly*
- *Methylphenidate: 10-80mg/day, 4-6 hourly*
- *Pemoline: 18.5mg increased to 148mg daily or bd*
  - *Olanzapine and Risperidone are expensive and not always available in developing countries.*
- *ART (if available) delays the onset and reduces the severity of AIDS-related dementia*
- *Correct nutritional deficiencies if possible*
  - *Vitamin B12*
  - *Vitamin B6*
  - *Folate deficiency*

Depression

The diagnosis and treatment of mood disorders are essential to the well-being of a patient infected with HIV. It is never appropriate to assume that a psychiatric symptom is simply an "understandable" reaction to the situation.

Depression is very common and often under-diagnosed and under-treated. Depression often increases over the course of illness, especially after the onset of AIDS.

Management of Depression

Treatment of depression and anxiety in a patient with advanced AIDS should be as active and rigorous as with any other medical illness. Depression is treatable and responds well to psychotherapy and medication, e.g.

Venlafaxine (37.5 – 150mg per day)
Amitriptyline (start 25mg and increase to 150mg nocté)
Fluoxetine (start with 10-20mg daily and increase to 80mg daily)

Even at the end of life, where a patient has a prognosis of only a few weeks, it may be appropriate to try a low dose of psychostimulant, e.g. Methylphenidate (from 10mg) or corticosteroid, e.g. Dexamethasone (from 2mg daily) to increase cognitive function.

In patients with associated agitation or anxiety, Risperidone (from 0.5mg daily) may be helpful.

Anxiety

Anxiety often co-exists with depression, but may also be caused by other reversible conditions (e.g: hypoxia, hypoglycaemia) medications (e.g. Isoniazid, corticosteroids, Theophylline) withdrawal of alcohol or drugs, excessive caffeine, etc.

Fear of pain, isolation, rejection, death and social issues such as child care and finances, cause anxiety and need to be addressed.

The treatment of anxiety includes the following options:

- *Psychotherapy and Psycosocial support*
- *Pharmacotherapy e.g: Clonazepam (1-4mg in divided doses)*
  Diazepam (2.5-5mg tds then 5-10mg nocté)
  Lorazepam (from 0.5-1mg to 6mg in divided doses)
  Buspirone (15-45mg in divided doses)
  Venlafaxine (from 37.5mg bd to 75mg bd)

Insomnia

Insomnia is distressing and exacerbates other symptoms associated with HIV/AIDS, such as pain, fatigue, memory loss and weakness.

Non-Pharmacological Management of Insomnia

- *Set sleep / wake times*
- *Exercise*
- *Reduce daytime napping*
- *Aromatherapy*
- *Reflexology*
- *Massage*
- *Psychotherapy and relaxation therapy*
- *Warm milk / herbal tea at night*
- *Avoid alcohol and stimulants at night*

Pharmacological Management of Insomnia

- *Benzodiazepines*
  - *Diazepam: 5-10mg nocté*
  - *Oxazepam: 10-15mg nocté*
  - *Lorazepam: 0.5-2mg nocté*
  - *Temazepam: 10-20mg nocté*
- *Antihistamines*
  - *Hydroxyzine 25mg nocté*
  - *Diphenhydramine 50mg nocté*
- *Tricyclic antidepressants*

Amitriptyline: 10-75mg nocté

NUTRITION AND HYDRATION IN A PATIENT WITH AIDS

Good nutrition is traditionally considered an essential component of the care of a person living with HIV/AIDS. Nutrition is provided with the primary intention of benefiting the patient. However, when a patient is approaching death, artificial hydration and nutrition are potentially harmful and may provide little or no benefit to the patient.

Cachexia needs to be differentiated from starvation. Starvation is deprivation of food leading to loss of weight, whereas Cachexia is a disproportionate depletion of lean body mass due to metabolic abnormalities. Feeding will not reverse the effects of Cachexia.

Cachexia in AIDS is caused by over-secretion of inflammatory cytokines which produce pathological changes including protein catabolism and loss of weight. Patients with AIDS also lose weight due to opportunistic infections, oral and esophageal infections, nausea, diarrhea, malabsorption and the side effects of medication.

In advanced AIDS, symptoms of thirst and hunger are reduced or absent. At this stage, supplementary feeding, intravenous or enteral alimentation should be avoided.

However, nutrition is a vital part of the management of all patients actively living with HIV/AIDS and

the following practical suggestions will maximize food intake:

- *Drink high energy drinks, e.g. maas, mageu, milk*
- *Eat small frequent meals*
- *Avoid alcohol*
- *Be as active as possible*
- *Eat food according to patient's own taste*
- *Eat a variety of food*
- *Make starchy food the basis of each meal*
- *Eat lots of fruit and vegetables (but avoid citrus fruit, pineapple and tomato if sore mouth or throat)*
- *Meat and dairy may be eaten daily (but decrease or avoid diary products if patient has diarrhea)*
- *Eat dried beans, peas, lentils, peanuts and soya regularly*
- *Include sugar, fats and oils*
- *Use salt sparingly*
- *Drink a lot of clean, safe water.*

With chronic vomiting, diarrhea and night sweats, dehydration is a serious concern, especially in hot climates. Easily prepared and affordable oral re-hydration solution should be taken:

Oral re-hydration solution:

- *1 litre clean, safe water*
- *8 level teaspoons sugar*
- *½ level teaspoon salt*
- *Mix well and store covered in a cool place.*
- *Make a fresh solution every day.*

Intravenous Re-hydration

Careful consideration needs to be given before starting intravenous re-hydration in a patient with end-stage disease in a Palliative Care setting.

In general, IV fluids help fatigue and orthostatic hypotension (dizziness). However, they are also associated with several adverse effects in the terminally ill, such as increased secretions, worsened cough, dyspnea and diarrhea. They can increase oedema and ascites and cause local complications of phlebitis and ecchymosis. They can also provoke symptomatic congestive cardiac failure.

It is important to note that the symptoms of thirst and dry mouth are usually not related to dehydration and are usually effectively managed by attention to oral hygiene and lip moisturisers.

Hypodermoclysis

Hypodermoclysis (subcutaneous infusion of fluid) is a simple and practical alternative to continuous intravenous hydration.

1-1.5 liters 0.9% saline or 5% Dextrose water can be infused subcutaneously into the abdominal wall over 24 hours via a "butterfly" needle.

Decisions about re-hydration need to be individualized and based on the wishes of the patient and their general condition.

PAIN MANAGEMENT IN AIDS

People with HIV disease often have multiple pains occurring concurrently and pain is often unrecognized and therefore widely under-treated in this population.

Various studies show patients with AIDS have on average 3 different sites of pain at any one time and up to a third of patients experience pain at four or more sites.

A study done on WHO Stage 4 AIDS patients in Soweto, South Africa, showed that over 90% of patients experienced pain and that the five common sites of pain were lower limbs (peripheral neuropathy), mouth, throat, headache and chest. Abdominal pain, joint, muscular and skin pains were also prominent.

Women with AIDS have unique pain syndromes of a gynecological nature related to infections e.g. Pelvic Inflammatory disease and gynecological malignancy, e.g. Carcinoma of the cervix.
The use of ART is one of the most effective means to control pain in AIDS; however, even patients who have received ART, continue to experience pain during the final stages of their lives.

Intensive educational programs need to be developed to provide education on the knowledge, skills and attitudes necessary for the effective management of pain in patients with AIDS.

Barriers to pain management in the developing world include lack of knowledge about HIV/AIDS, Palliative Care and pain control, as well as lack of access to essential analgesics or pain management specialists. Unfounded fears regarding the use of potentially addictive drugs contribute to the problem.

Optimal management of pain in AIDS requires a multidisciplinary approach and a thorough knowledge of the use of the WHO analgesic ladder. This includes the adjuvant analgesics that play a key role in the management of AIDS-related pain.

WHO Three Step Analgesic Ladder (See Chapter 8)

Health care professionals should be comfortable with the use of one or two medications on each step. If the prescribed drugs do not produce adequate analgesia, treatment is escalated in an orderly manner, from non-opioid to weak opioid to strong opioid. Analgesics for chronic pain should be given "by the mouth" (orally) if at all possible, "by the clock" (regularly) and "by the ladder" (WHO analgesic ladder).

Weak opioids should not be combined with strong opioids. Non-opioids may be combined with weak or strong opioids.

Adjuvant analgesics can be added to any step of the ladder and are very useful in many AIDS-related pain syndromes.

Examples of Adjuvant Analgesics used in AIDS

- *Tricyclic antidepressants*
  - *Amitriptyline for Neuropathic pain*
- *Anticonvulsant drugs*
  - *Carbamazepine for Neuropathic pain*
- *Corticosteroids*
  - *Dexamethasone for inflammation, edema, bone and neuropathic pain*
- *Benzodiazepines*
  - *Diazepam for muscle spasm and tension headache*
- *Antispasmodic*
  - *Hyoscine butyl bromide for colicky abdominal pain*

It is important to attempt, as far as possible, to diagnose and treat the actual cause of pain. Pain is also influenced and altered by the patient's mental and psychological state and so the care of pain goes beyond drug treatment alone.
Counseling and non-pharmacological measures such as Trans Electrical Nerve Stimulator (TENS), acupuncture, physiotherapy and aromatherapy are important considerations.

Common Pain Syndromes:

Oropharyngeal Pain

The most frequent causes include:

- *Oral candidiasis*
- *Apthous ulceration*
- *Herpes simplex infection*
- *Gingival and periodontal disease*
- *Salivary gland disease*
- *Kaposi's sarcoma*
- *Dental abscesses*
- *Cytomegalovirus infection*
- *ddc stomatitis*

Management of Oral Pain

Oral pain is so common in patients with AIDS and topical analgesia can be used together with systemic analgesics.

- *Local anesthetic and local inflammatory agents applied directly to painful areas*
  "Xylocaine" spray Benzydamine mouthwash
  Choline Salicylate "Teejel"
- *Corticosteroids are useful for treating painful apthous ulcers*
  Beclomethasone spray (use the "asthma pump")
  Triamcinolone paste ("Kenalogg in orabase")
- *Coating/Protective agents:*

Carmellose paste "Orabase"
Sucrulfate suspension "Ulsanic"
"Mucaine" (Oxethazaine, Aluminium Hydroxide, Magnesium Hydroxide)

Esophageal Pain

Possible causes of Esophageal Pain

- *Candidiasis (not always associated with oral disease)*
- *Apthous ulceration*
- *Cytomegalorvirus*
- *Herpes simplex*
- *Kaposi's sarcoma*
- *Lymphoma*
- *Mycobacteria*
- *Zidovudine, ddc and NSAIDS can cause oesophagitis*
- *Reflux oesophagitis*

Management

The control of retrosternal pain in the Palliative Care setting is often empirical with the use of antacids or H2 receptor antagonists, treatment of candidiasis with ketoconazole or fluconazole, and a combination of opioids, NSAIDS and/or paracetamol. If available, oral acyclovir should be prescribed if symptoms persist. If a nasogastric tube is required, it should be a temporary measure, only until a patient is able to swallow once more. Nifedipine (5-20mg) or hyoscine butylbromide (10-20mg) may relieve esophageal spasm.

Chest Pain

Chest pain may be caused by esophageal, cardiac, lung, pleural and chest wall conditions.

Possible Causes of Chest Pain

Respiratory infections, e.g. PCP, Pulmonary TB, bacterial pneumonias
Varicella Zoster and Post Herpetic Neuralgia
Tumors, e.g. Kaposi's sarcoma,
Non-Hodgkins' Lymphoma
Pleuritis / Pericarditis
Esophageal candidiasis, apthous ulceration, CMV and herpes.

Management

The palliative management of chest pain includes treating the underlying etiology wherever possible, using the WHO analgesic ladder and non-drug therapy, e.g. physiotherapy.

Abdominal Pain

In the immunosupressed patient, abdominal pain is frequently a marker of opportunistic infections.

Causes of Abdominal Pain:

- *Pelvic inflammatory disease usually caused by Neisseria gonorrhoea, Chlamydia trachomatis with*

or without secondary infection with E Coli, Bactericides fragilis and streptococcus faecalis.

- *Infections (enteritis/colitis) caused by Cryptosporidiosis, shigella, salmonella, campylobacter, CMV, HIV itself, MAI etc.*
- *Lymphoma and Kaposi's sarcoma of the gastrointestinal tract*
- *Ileus*
- *Organomegaly*
- *Cholecystitis and sclerosing cholangitis may be caused by CMV or cryptosporidiosis*
- *Opportunistic liver infections by CMV, TB, MAI and Cryptococcosis, Histoplasmosis, viral hepatitis (Hepatitis B or C) and Pneumocystis Carinii*
- *Drug-related hepatic toxicities from ddi, pentamidine, ritonavir and nevarapine, isoniazid, pyrazinamide and nifampicin, co-trimoxazole and azole antifungals*
- *Pancreatitis may be caused by antiretrovirals such as ddi, stavudine (d4T), ddc as well as CMV, MAI and cryptococcal infection.*
- *Herpes Zoster*
- *Spontaneous aseptic peritonitis*
- *Toxic shock*
- *Fitzhugh-Curtis Syndrome*
- *Disseminated TB*

Management

Patients may present with a wide range of abdominal pains, ranging from right upper quadrant pain to cramps, bloating, generalized peritonism or localized peritonitis. Fever is commonly associated and diarrhea often present.

In the patient with far advanced disease, there is little place for specific investigation and therapeutic intervention as general symptomatic management using the WHO analgesic ladder is usually more effective.

Perianal and Genital Pain

Possible causes of Perianal and Genital Pain:

Infections:
Herpes simplex infection type I or II
Neisseria gonorrhoea
Chlamydia trachomatis
Vulvovaginal Candidiasis
Human Papilloma virus
Fissure-in-ano and inflammatory strictures
Haemorrhoids aggravated by diarrhea
Perianal abscesses and ulceration
Proctitis
Anorectal carcinoma, Kaposi's sarcoma or squamous cell carcinoma
Exoriation due to chronic diarrhea

Management

Repeated cultures and biopsies often fail to demonstrate infection or malignancy, and chronic perianal and genital disease are a frequent cause of morbidity in AIDS patients.

It is reasonable in the Palliative Care setting to treat empirically and to provide local and systemic pain relief and stool softeners. A variety of preparations containing local anesthetic and corticosteroid are available for rectal use. Empiric treatment includes acyclovir for herpes simplex, amoxycillin for gonococcus and tetracycines for chlamydia.

Rectal spasm can be managed with Nifedipine (5-20mg) or Hyoscine butylbromide (10-20mg tds) or Chlorpromazine (10-50mg tds.)

Neurological Pain Syndromes

Headache

Headache is very common and can be caused by a wide range of conditions from mild and benign to life-threatening, e.g.

- *Intracranial infections, e.g. toxoplasmosis, cryptococcal meningitis, HIV, encephalitis and meningitis*
- *Intracranial tumors*
- *Migraine*
- *Tension headache*
- *Sinusitis*
- *Side effects of antiretrovirals, e.g. AZT*

Peripheral Neuropathy

The most common peripheral neuropathy seen in patients with AIDS is a painful symmetrical predominantly sensory neuropathy caused by HIV itself. Patients complain of numbness, tingling, burning, pins and needles and shooting pains usually in the soles and dorsum of the feet.

Other causes of neuropathy in a patient with HIV/AIDS are:

- *Varicella Zoster with Post Herpetic Neuralgia*
- *Toxic Neuropathy (e.g. alcohol)*
- *Nutritional deficiencies (e.g. Vitamin B6 and B12)*
- *Other infections (e.g. CMV, MAI and Syphilis)*
- *Diabetic neuropathy*
- *Antiretroviral drugs can cause painful toxic neuropathies e.g. ddi (didanosine), ddc (Zalcitabine) and d4T (Stavudine)*
- *Other drug-related neuropathies (e.g. Isoniazid (INH), Ethanbutol, Vincristine, metronidazole)*

Management of Neuropathic Pain

Optimal management of neuropathic pain involves the use of the WHO analgesic ladder including the non-opioid and opioid drugs and the addition of any of the following adjuvant analgesics:

- *Tricyclic antidepressants*
  -Amitriptyline:10-150mg nocté
- *Anti-convulsants*
  -Carbamzepine: start 100mg bd, increase to 1600mg / day
  -Valproate: 200-1200mg per day
  -Phenytoin: up to 300mg daily
  -Gabapentin: 100mg tds. Increase up to 3600mg daily
- *Membrane stabilizers*
  -Flecainide: 100-200mg bd
  -Lignocaine: subcutaneous infusion or IV infusion

Rheumatologic Pain Syndromes

Patients with HIV/AIDS are vulnerable to varying forms of arthritis, arthralgia, arthropathy, myositis, myopathy and myalgias.

The arthritis may be related to HIV itself, psoriatic, reactive (Reiters) or septic. Reactive arthritis to Chlamydia infection is the most common arthritis seen with HIV infection. Muscle pain is very common and could be caused by HIV itself or related to Zidovudine, Pyogenic infection (usually Staphylococcal) or Microsporidiosis.

Musculoskeletal infections in HIV positive patients can cause severe pain, e.g. Osteoarticular TB.

- *Septic arthritis and acute osteomyelitis (often caused by Staphylococcus aureus)*
- *Cellulitis and bursitis (often caused by Stafylococcus aureus and Streptococcus pyogenes)*
- *Soft tissue abscesses*

Generalized Body Pain

Generalized body pain is common in a patient with advanced disease and is often related to wasting and immobility.

Patients present with severe skeletal pain that is worse on movement and may or may not be associated with diffuse skin pain.

NSAIDS and/or opioid drugs may be effective for these patients.

Wound Pain

Management of Wound Pain:

- *Systemic analgesia using the WHO analgesic ladder*
- *Treat infection e.g. Metronidazole gel/paste topically, systemic antibiotics*
- *Topical anaesthesia e.g.*
  — Dressings soaked in Lignocaine or morphine
  — Morphine or lignocaine ampoules mixed into a carrier
  Medium such as Intrasite gel or UEA cream

Corticosteroids

There is understandable concern about the use of corticosteroids in a patient with AIDS due to potential acceleration of opportunistic infections in an immunocompromised patient.

However, there is value in the use of steroids in the Palliative management of disseminated TB or MAI, severe apthous ulceration, severe dyspnea, neuropathic pain, musculoskeletal pain, uncontrolled fever and sweating, headache from raised intracranial pressure, loss of appetite, energy and well-being. Doses used are often in the low range (Dexamethasone 2-4mg/day) with minimal, if any, adverse effects.

There is little evidence that corticosteroids have a deleterious effect on infections in patients with advanced stages of disease. However, the use of prophylactic anti-fungal therapy, whilst a patient is on a corticosteroid, is recommended.

In advanced AIDS, the benefits may far outweigh the risks of corticosteroids

COMPLEMENTARY AND ALTERNATIVE THERAPIES

ART is not always available in the developing world and patients may have resource to alternative, complementary and/or herbal medicines.

Many herbs such as Echinacea, European Mistletoe, Licorice, plant sterols/sterolins from the plant extract Hypoxis, Sutherlandia Frutescens and even Cannibis have been used by patients with HIV/AIDS.

In Africa, patients are know to use Cannibis for pain control, reduction of nausea and a sense of wellbeing, usually in the form of a 'tea'.

There is a dire need for more research in the fields of efficacy, mechanism and interactions of these complementary/alternative agents.

A guiding principle for any practitioner is that proven therapies should never be undermined by experimental ones, and that if alternative therapies are excessively expensive or cause adverse effects, they should be used with circumspection.

RECOGNISING THE DYING PATIENT

One of the biggest challenges in caring for a patient with AIDS is the unpredictability of disease progression. Although AIDS is a fatal illness with life-threatening opportunistic infections, malignancies and progressive neurological disease and wasting, in most cases inter-current illnesses are interspersed with periods of relatively stable health.

It is difficult to prognosticate and even more difficult to recognize when a patient is dying. In this respect, AIDS is different to cancer.

The distinction between potentially curative and Palliative Care is blurred and the unexpected often does happen. Often patients dying of AIDS are young and acceptance and understanding of death is difficult. The dying process may be short-lived or take many days.

In general, the more frequent, severe, or varied the infections, the poorer the prognosis. Clinical signs and symptoms often associated with decreased survival time include:

- *Poor performance status > 50% of day in bed*
- *Chronic diarrhea and rapid loss of weight or wasting*
- *Progressive cachexia with loss of > 30% lean body mass*
- *Neurological manifestations e.g. fatigue, lethargy, confusion, paralysis*
- *Progressive multifocal leucoencephalopathy*
- *Decreased response to ART or viral resistance to ART*
- *Rapid disease progression/severe deterioration*
- *AIDS-related malignancy e.g. Kaposi's Sarcoma, lymphoma*
- *CD4 count <200/mm3*
- *Serum albumin <30g/L*
- *Hypoxia*
- *End organ failure (renal, hepatic or cardiac failure)*

Several psychosocial factors are associated with decreased survival time:

- *Physical or emotional exhaustion of social support*
- *Increased demands on the caregiver*
- *Hopelessness or "giving up" on the part of the patient; a desire of patient for death.*

Withdrawal of Therapies

Polypharmacy for patients with AIDS is common as disease progresses. Redefining goals of care will help to simplify the patient's drug therapy.

It is very difficult to issue guidelines concerning which treatments can be withdrawn as a patient becomes more terminal. In general, organism-specific prophylactic treatment should continue as long as the patient is willing and able to swallow medication, as the morbidity of these conditions is high e.g:

- *Prophylaxis for pneumocystis carinii pneumonia and toxoplasmosis*
- *Prophylaxis for Herpes Simplex infection*
- *Prophylaxis for Cytomegalovirus retinitis*
- *Treatment and prophylaxis of oral and esophageal candidiasis*
- *Treatment of transmissible infections, e.g. Tuberculosis*

However, with certain infections drug therapy should be stopped if :

a) The treatment has no benefit on survival of the patient

b) Symptoms of the disease have failed to regress or have recently progressed in spite of treatment;

c) Treatment is associated with drug toxicity and/or inconvenience;

d) The patient chooses to stop treatment.

Any decision to withdraw medication will depend on the patient's goals and the appropriateness of therapy in the individual patient.

It should be noted that symptomatic progression of opportunistic infections does not necessarily occur after stopping treatment. The Palliative management of symptoms of Mycobaterium avium infection with NSAIDS and corticosteroids may be better tolerated that multiple antibiotics in patients with advanced disease.

As Death Approaches

- *Review medication*
- *Discontinue non-essential drugs*
- *Continue analgesics, anti-emetics, anti-convulsants and sedatives only*
- *Rehydration may not be beneficial in all patients*
- *Pay attention to secretions, mouth care and skin care*
- *Explanation to relatives*
- *Change route of medication if necessary, e.g. oral to subcutaneous route*
- *Rely on clinical findings rather than investigations: "Treat the patient, not the blood tests."*
- *All care and effort should be focused on quality of living and quality of dying*
- *Ensure companionship and reassurance*

It is important to accompany patients through illness until death, and not see death as an automatic failure of the clinician, to appreciate the profound importance of 'being there' and of understanding our role as 'caring' and not necessarily 'curing'. As written by Sheila Cassidy, a British Hospice Physician, in her *Sharing the Darkness: "Slowly, I learn about the importance of powerlessness. I experience it in my own life and I live with it in my work. The secret is not to be afraid of it – not to run away. The dying know we are not God. All they ask is that we do not desert them."*

PSYCHOSOCIAL ASPECTS OF CARE IN HIV/AIDS

It is impossible to understand a patient without understanding his or her culture and ethnicity. There are considerable cultural variations between people of different faiths, ethnic backgrounds, and national origins in their approach to terminal illness. Culture therefore incorporates the whole of palliative care for example, coping with pain, diet, modesty, communication, death and bereavement rituals. In a developing context like South Africa, respect for the unique culture and ethnicity of the patient and his or her family is paramount, if we are to provide effective palliative care. The practice of palliative care also differs according to culture, for example, in a Western world; the palliative care team is more narrow based consisting of health professionals and volunteers. Whereas, in a developing, African world, the team is more broad based consisting of family, extended family, village, community, and traditional healers. This is further emphasized when working with HIV/AIDS, as it is in itself a disease clouded in stigma, superstition, myth and misconceptions. In order to practice culturally sensitive palliative care, we, as care providers, need to carefully examine our own prejudices, assumptions and cultural beliefs, as only then will we be able to fully understand and respect the uniqueness of our patients. In addition, experience with cultural diversity has also

taught us that depersonalization occurs, when we try and put those people who are different from oneself into categories, because somehow their differences are easier to deal with if they seem to belong to a group with clearly defined norms. It is imperative therefore that, however much the carers know about other cultures and religions and their attitudes to palliative care, they ask the patient for his or her preferences, and encourage communication about the differences in his or her religion and culture. This requires a relationship of a different kind from the usual one between carer and patient. But it is an extraordinary opportunity for both sides to learn about other traditions, other interpretations, and other acceptances. It can lead to a level of human understanding hard to reach when carers and patients come from the same broad religious and cultural group, where the traditions are already, assumed to be given. This can also provide a moment when the patient is fully in control, since they have valuable information that the carer does not have.

AIDS DEATH IN A DEVELOPING WORLD

More often than not, AIDS is regarded as an untimely as well as a bad death, because of the age of those who are dying and especially the social and economic impact of youthful death. The causes and timing of death only partly influence the way people understand and respond to death and dying. Experiences and perceptions of death are also complicated by their social consequences. Death is a socially complex process that has an impact over time and space that extends far beyond the dying individual and the event of death itself, as is the case with HIV/AIDS.

Significant developments and advances in the bio-medical world have influenced social and cultural responses to death. One outcome has been to place death and dying in the hands of hospitals and the medical profession. This has major implications for developing countries and in turn palliative care, as AIDS presents as far more than a biological disease, but rather a disease of social, cultural and economic consequences for those infected and affected. Hence, the need for palliative care in the developing world is overarching, especially in light of the lack of patient-centered medical and hospital care. Thus, in the developing world, the pre-eminence of the biomedical model in shaping our responses to managing terminal illness is tempered by people's parallel pursuit of traditional medicine, which includes spiritual healing and home-based care. Given this dual system of explanation and treatment, the debate around the scope and limits of professional care needs to be broadened to encompass palliative care, care for the whole person, and for his or her loved ones.

In broadening our conceptualization of a 'good death' or a 'bad death', the palliative approach to an AIDS death can be a dignified, empowering, and culturally sensitive practice, which affords the human being the opportunity to die in a the manner that is unique and appropriate to him or herself.

"Dying is a very emotional and personal experience. It is also a very social process. There are social expectations about how the dying and those around them should respond to death, and these are articulated and acted out through social institutions developed to respond to death. By force or by choice, these are being made to adjust to the modern day context of death- namely AIDS. The impact on individuals and institutions will vary, but none will remain unaffected".

COUNSELLING/SUPPORT IN PALLIATIVE CARE

Palliative care has long recognized the need for psychosocial support of patients and their families. In developing world, psychosocial support extends far beyond patients and families' psychological needs, as care providers have to assist patients with their practical needs such as food, grants and placements. Hence, counseling and support occurs on many levels and involves a number of tasks. *Supportive, client-centered helping* means that the needs of the client are central and that the ultimate purpose of the process is to identify and implement actions that will improve the client's situation. The AIDS epidemic, more than any other, has brought with it the need for health care workers to have basic counseling skills. AIDS counseling can occur along the entire continuum of care: from pre-test counseling, to post-test counseling and working through a positive diagnosis, to how to manage and live with the disease, to working with end of life issues and then bereavement counseling for the family, following the death of a loved one to AIDS.

HIV/AIDS counseling and support can be long term or short term and has two general aims, namely:

- *The prevention of HIV transmission and re-infection, and*
- *The support of those affected directly and indirectly by HIV/AIDS.*

These broad aims are interwoven into the psychosocial aspects of AIDS within a palliative model of care, which focuses on total patient care- medical, psychological, social, spiritual and cultural needs of the patient and his/her family.

In our experience of working with AIDS patients, the following issues and needs are apparent in the experiences and needs of the patient and family members:

- ***Fear****- Both the infected and affected have many fears. They are particularly fearful about being isolated and rejected. They are afraid of the uncertainty of the future and most importantly, they are afraid of dying and of dying alone. As the majority of AIDS patients are young adults with young families, there is also an overwhelming fear around leaving loved ones behind.*
- ***Loss****- AIDS patient's experience multiple losses through their illness. They experience loss of control, loss of autonomy, loss of physical abilities, loss of relationships, loss of status, loss of financial security and independence. The list is painfully endless and each new day presents itself with numerous losses to be faced. Most significantly is the fear of losing ones ability to care for oneself and ones family, and the loss of life itself.*
- ***Grief****- AIDS patients experience profound grief about the losses they have experienced and are anticipating. They grieve for those who have died from AIDS, and they grieve with and for their loved ones- those who must stay behind and try to cope with life without them.*
- ***Guilt****- Guilt and self-reproach for having contracted the virus, possibly infecting others and for having to die are frequently expressed by AIDS patients. There is also guilt about the sadness that the illness will inflict on loved and families- especially children.*
- ***Anger****- AIDS patients are often angry at themselves, at life and at their situation, and this anger is often taken out on those closest to them. They are angry because there is no cure, and at society's attitude towards the illness.*
- ***Anxiety and depression****- The chronic uncertainty associated with the progress of the infection often aggravates feelings of anxiety and depression. This is further compounded by feelings of*

having lost so much in life, and having to lose life itself.

- ***Spiritual concerns**- Palliative care acknowledges the existential distress experienced by patients, who are confronted with death, loneliness, and physical and psychological suffering. Existential distress is probably the least understood source of suffering in patients with advanced disease, for it deals with questions regarding the meaning of life, the fear of death, and the realization that they will be separated from loved ones. These issues take on greater importance in HIV/AIDS because of the stigma and judgment that still accompany individuals living with the disease.*
- ***Socio-economical issues**- Socio-economic and environmental problems often contribute to the psychosocial needs of the patient and his/her family. This is particularly true in the developing world, as patient's basic needs are often not met due to high levels of poverty and unemployment. Hence, the role of the caregiver may involve: arranging food parcels for patients, organizing placement for the patient to live, applying for disability grants, ensuring that children are taken care of, and even arranging transport for a patient to return to his/her homeland to die.*

The basis then of psychosocial support is compassion, respect, patient self-determination, and being present in the midst of our patients suffering. By being present and caring for our patients, we connect to them as individuals. The interconnectedness at the level of our humanity helps to provide hope and comfort to our patients. By providing our patients with comfort, care and support, we provide them with the opportunity to 'heal' and to manage their situation on all levels of need.

The significant others in the patient's life play an important role in the person's physical and psychological care. Furthermore, it has been found that in developing countries, the family is the main site of care giving of the terminally ill and of those who survive their demise. But these people often themselves need help to come to terms with:

1) their own fears and prejudices and

2) the implications and consequences of their loved one's sickness and ultimate death. Care providers can therefore play a significant role in supporting family members with the physical and emotional care of their loved one. Affected significant others experience similar psychosocial feelings as does the patient- the same feelings of anxiety, depression, loss, fear, uncertainty and grief.

BEREAVEMENT (SEE ALSO CHAPTER 4)

The palliative care team can provide support to the family and significant others by assisting them in coping with the illness on a day to day basis, as well as with bereavement issues following the death of their loved one. Hence, **bereavement i**s also an important component of palliative care, and has unique features in terms of AIDS:

- *Status*
- *Multiple losses*
- *AIDS orphans and vulnerable youths*
- *Substance abuse*
- *Effects on households: most of the AIDS deaths in our society are adults aged between 20 and 40 years. This has severe implications on families as they are losing young mothers, breadwinners and carers. A unique feature that we are experiencing is the effects on grandmothers who are being left with the responsibility of caring for their grandchildren. It is ironic that the caregivers*

who are also elderly grandparents have to provide economic support for the orphans. This is unexpected because the grandparents in the past depended on the children's parents for assistance in their old age. Hence, focus is now being given to this generation, by empowering grandparents with the necessary skills to carry out these new responsibilities.

Generally, with the exception of war and accidents, death in many parts of the globe has become the prerogative of the old. In this, South Africa and other societies which are variously described as underdeveloped or developing are similar, even though death comes more frequently and earlier. Now, AIDS is radically reorganizing the demography of death, because as Frankenberg pointed out a decade ago, AIDS strikes at people who are in their procreative and productive prime. It interrupts the way contemporary societies have come to organize around the life cycle, as has been shown.

The main task of bereavement work is to help the bereaved work through the pain of the loss and to integrate the loss into their lives so as to begin moving on with life. This process is both emotional and in a third world setting also practical, as bereaved families may need assistance with income, skills and resources. Due to the intensive nature of palliative work, the team plays an integral role in the support of the patient and his/her family during and after the death, and as a result of this involvement, we remain a source of support long after the death.

FURTHER SHIFTS

The socio-economic situation in developing countries has required that palliative care professionals and organizations meet many new challenges that have in turn influenced the vision and mission into new spheres. For example, education and prevention, support groups, income generation projects, support and assistance to vulnerable children and grandparents, and on some level poverty alleviation. Therefore, it is recommended that in the developing world, intervention needs to be multi-faceted, proactive and purposive.

The above has also necessitated a further paradigm shift from institutional care to an emphasis on Home-Based Care (HBC). The aim of HBC is to provide patients and families with palliative care within their home environment. The focus is therefore on empowering community members, families and friends to provide care to those infected and affected by AIDS. The role of the team is to provide guidance, education and support to care providers so that their loved ones can be cared for adequately at home. This shift towards HBC has a major advantage in developing countries as it alleviates the enormous cost of hospital and institutional care.

CAREGIVER BURDENS

The changing demographics of the AIDS epidemic, along with the growing complexity of medical care, have created major challenges for the health professionals who provide curative and palliative care and the informal caregivers who provide emotional and practical support to relatives and friends living and dying from HIV/AIDS. Providing palliative care in a developing context intensifies the emotional and physical demands of caregivers. Caregivers, both formal and informal, face the added burdens of poverty, inadequate housing, lack of available resources, inadequate health care, poor sanitation, physical demands, emotional issues surrounding the illness and death, and lack of knowledge, power

and information. Psychologists use the term "caregiver burden" to describe physical, emotional, financial, and social problems associated with care giving. Due to these factors, the palliative team needs to be aware of one another and how others are managing, as caregiver burnout has serious consequences for the caregiver, care recipient, and health care system. Thus care giver burnout is a two pronged issue for the team and the organization, as attention and care needs to be given to the informal carers of people dying from AIDS, as well as looking at ways to manage and counteract burnout within the team and organization. These include in-service training, supervision, counseling, on-site health-promotion programs, and setting realistic work and personal goals.

CONCLUSION

"The best time to plant a tree is twenty years ago……..The next best time is now."
(An African proverb)

A mere two decades ago HIV/AIDS was unknown. Today HIV/AIDS covers the world in dark clouds of fear, uncertainty and suffering. HIV/AIDS has presented so many challenges and has brought about so many unanticipated changes. AIDS has a tremendous impact both on the medical, psychological, social, spiritual, educational and economic life of the infected person; his or her affected others and the community as a whole. All this places a tremendous burden on the shoulders of health care professionals who need to offer infected individuals and their significant others complete and dedicated services which exceed the customary bounds of conventional medical care and treatment. This situation has called for health care professionals working in the field of HIV/AIDS and providing palliative care, to become a comprehensive caregiver, adviser, educator and counselor in diverse cultural and social contexts.

The common clinical spectrum of AIDS is broad, covering a range of opportunistic infections, malignancies and neuropsychiatric disturbances. The use of specific therapy is important for control or prophylaxis of infections. Antiretroviral treatment is the best form of Palliative Care available for AIDS, but the Palliative control of pain and symptoms is essential regardless of whether patients receive active therapy or not.

Palliative Care of a patient with AIDS goes beyond the medical care to include unique problems with social support, emotional support and bereavement.

In the case of someone with AIDS, it is the meticulous attention to detail, the degree of communication between all concerned, and the teamwork with compassion and understanding which will make the ultimate difference to the quality of living and dying; these are the factors too, which will shape the memories of the patient's loved ones.

The essence of this chapter is to make a small contribution towards the empowerment of individuals from various professions and disciplines so that they can make a difference- and plant a tree of hope and healing right now. The Zulu word "Ubuntu" captures the essence of palliative care and the role that it can play in the developing world's plight in facing the challenges of HIV/AIDS. "Ubuntu" means together as one, a collectivity and connectedness of human beings. In light of this, palliative care can play an enormous part in this epidemic, as it encapsulates the very principles of caring without cure,

and of working together toward the comfort and care of individuals infected and affected by AIDS.

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11 Tuberculosis

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INTRODUCTION

Tuberculosis (TB) causes a great deal of ill health in most low-income countries. Epidemiological data on tuberculosis in industrialised countries is good and will continue to improve. The world problem of tuberculosis now lies in a large group of developing countries (population of about a milliard) where there is virtually no decrease in the annual risk of tuberculosis infection with all of its consequences. There is strong evidence that tuberculosis could be controlled in these countries (1). In 1995 more people died of TB than in any other year in history. It is estimated that thirty million people will die from tuberculosis between 1995 and 2005 if current trends continue (2). TB is the most common cause of death in individuals aged fifteen to forty-nine years.

In the last decade, factors contributing to the seriousness of the disease were found to be poor socio-economic conditions in large parts of the society, unemployment, overcrowding, alcohol abuse, malnutrition and an increase in the rate of HIV/AIDS infections. The economic burden on the healthcare sector is substantial. The fight against TB is a public health problem and is the direct responsibility of government health authorities. For TB control to be successful, health authorities require assistance from other healthcare organisations. This chapter describes the disease and challenges of tuberculosis, including diagnosis, treatment and palliative care.

TB poses a serious and increasing problem for most developing countries and affects the health and social welfare of large proportions of society. Thanks to modern antituberculosis medications, it is possible to cure practically all patients suffering from this potentially fatal disease. Successful treatment, however, requires adequate medication, close supervision by staff, direct observation (control) of drug ingestion and the monitoring of the treatment with regular bacteriological testing. If these preconditions are met, TB control is a cost effective health intervention. Once identified, TB can be treated and will rapidly become non-infectious. TB can be cured in almost 95% of all

cases, including individuals infected with HIV. TB is increasingly becoming impossible to cure due to careless treatment practices that cause the bacterium to become resistant to previously effective drugs. Multi-drug-resistant TB has the potential of throwing humanity back into the era when the diagnosis of TB was tantamount to a death sentence. Only humans develop multi-drug-resistant TB. It develops when doctors, or other health workers, prescribe the wrong drugs or the wrong combination of drugs. Drug resistance may also occur if the correct anti-TB drugs are not taken for the entire six months of treatment. No physician should prescribe powerful TB drugs without ensuring that they are correctly taken. In poor and developing countries, patients with multi-drug-resistant TB usually die because effective treatment is often impossible. Even in wealthy countries up to half of multi-drug-resistant patients die of TB because of the expense and difficulty of treatment. The costs of treating a multi-drug-resistant TB patient can be one hundred times that of a non-resistant patient. Multi-drug-resistant TB can also spread to other people just as easily as regular TB. The incidence of multi-drug-resistant TB increases exponentially with every poorly, or inappropriately treated, patient.

Although many children are infected with the TB microorganism, the most affected group is between 15 and 45 years old and is the economically active part of the population (3).

In Africa, the most infectious, and the most common, form of TB is sputum smear positive pulmonary TB, often called "open TB". In Namibia 85% out of all TB patients suffer from pulmonary TB, and more than 50% of these patients are sputum smear positive (3). These individuals not only suffer personally from the disease, but if they remain untreated pose a infectious threat to their relatives and neighbourhood. These individuals need to be identified and treated as a priority risk group, the control of which will finally reduce the infectious pool.

The aims of the fight against TB are:
For individual patients:
- *To cure their disease,*
- *To restore quickly their capacity for activities of daily living*
- *To preserve their position in the family and community they belong to.*

For a community:
- *To decrease the spread of TB infection*
- *To eradicate the disease from the society*

Considering the priorities of anti-TB activities, the identification, treatment and cure of TB patients is the first priority with special consideration given to those who are the source of transmission of the infection.

TB can only be controlled successfully, and eventually eradicated, in the context of a National Tuberculosis Control Programme (NTCP).

TB DEFINITION

TB is an infectious disease that in most cases is caused by a microorganism called Mycobacterium tuberculosis. The microorganisms usually enter the body by inhalation into the lungs. The infection

can spread from the initial location in the lungs to other parts of the body via the blood stream, the lymphatic system and the airways, or by direct extension to other organs [3].

Pulmonary tuberculosis (PTB) is the most common form of the disease, occurring in over 85% of all cases in developing countries. It is the only form of TB that may be infectious (in case of open pulmonary TB with infectious sputum).

Extra-pulmonary tuberculosis affects organs other than the lungs, most commonly pleura, heart, lymph nodes, spine, joints, genital-urinary tract, nervous system or abdomen. However, TB may affect any part of the body.

TRANSMISSION OF INFECTION

TB develops in the human body in two stages:

- *Stage one: an individual is exposed to microorganisms from an infected person (primary TB infection)*
- *Stage two: the infected individual develops the disease (TB).*

The infectiousness of a case of TB is determined by the concentration of the microorganisms within the lungs and their spread into the air surrounding the patient who has the disease. Patients with PTB in whom microorganisms are found on microscopic examination of the sputum (smear positive cases) are the most infectious cases.

Those in whom microorganisms cannot be seen directly under the microscope (smear negative cases) are much less infectious, and the severity of their disease is usually less than that of the smear positive cases. Extra-pulmonary cases are almost never infectious, unless the patients suffer from PTB as well.

The infectious patient with PTB expels microorganisms into the air in tiny droplets during coughing, laughing, sneezing or spitting. These small droplets dry rapidly, become droplet nuclei harbouring the microorganisms that may remain suspended in the air for several hours. Studies show that TB bacteria remain alive up to three years in closed environments. Anyone in close contact with an infectious individual may inhale these droplet nuclei containing the microorganisms. While TB bacteria travel easily through the air, they proceed more slowly once inside a person's body. If the microorganisms establish themselves in the lungs of a person who inhaled them, they then multiply and the infection begins. This is how infection spreads from one person to another. Exposure to the TB microorganisms is greatest among those living in the same house with an infected person. Overcrowding and poor ventilation will increase considerably the risk of transmission.

In pulmonary TB, bacteria gradually destroys the lung tissue. They eat holes in the lungs and pus accumulates as the body struggles to fight the infection. Blood vessels may become eroded and rupture into the infected lung cavities and airways producing bloody sputum.

TB AND THE HUMAN IMMUNODEFICIENCY VIRUS (HIV) (SEE ALSO CHAPTER 10)

HIV infection is spread most commonly by sexual intercourse, exchange of blood or blood products and from mother to child. Infection with HIV leads to extensive destruction of the immune defence system of the body. As a result, those infected with HIV become ill with severe and mostly deadly diseases in contrast to persons without HIV. When the patient with an HIV infection also has an "opportunistic" disease, the affected person is said to have the Acquired Immunodeficiency Syndrome, or AIDS. For additional information on HIV, please see chapter 13 of this publication.

The development of TB is usually prevented by the a person's immune system which explains why only a relatively small proportion of exposed healthy individuals go on to become ill with the disease. In individuals in whom the immune system has become compromised by an HIV infection, TB can easily develop either from exposure to the bacteria or as the result of the release and multiplication of microorganisms that had been dormant, and held in check, by the formally effective immunological system. Pulmonary TB is still the commonest form of TB in HIV infected patients. The presentation of the disease depends on the degree of immune suppression (4, 5).

The HIV epidemic has increased the burden of TB, especially in populations where the prevalence of TB infection is high among young adults. For a person dually infected with both HIV and M. tuberculosis, the lifetime risk of developing TB is about fifty percent. The increased number of potential TB cases leads to an increase in the transmission of TB microorganisms within the community. It is imperative to rapidly identify and treat all infectious cases of TB in order to reduce its spread.

As in adults, the natural history of TB in a child infected with HIV depends on the stage of the HIV disease. Early in the HIV infection, when immunity is still good, the signs of TB are similar to those found in a child without HIV infection. As HIV infection progresses and immunity declines, dissemination of TB becomes more common. The HIV epidemic heightens the need to focus on the identification and cure of infectious TB patients. These dual epidemics of TB and HIV/AIDS have become the most serious public health threat of the decade.

CASE DEFINITIONS

Before the question of case detection and diagnosis is answered, TB case definitions have to be clear. The following terms are used in many countries that have a National Tuberculosis Control Programme (NTCP):

- *Direct microscopy positive (DM +) PTB*
  The patient produces sputum, which on direct microscopy shows tubercle microorganisms. This type is also called slide positive, acid fast bacilli (AFB) positive or sputum positive TB:
- *Direct microscopy negative (DM-) TB*

Patients with general complaints such as ***fever, weight loss, night sweats, cough, and chest pain*** have symptoms that are all compatible with the clinical picture of PTB. The chest X-ray must show signs indicative, or suggestive, for PTB. The sputum does ***not*** reveal microorganisms on direct microscopy. Patients, who are culture positive, are also classified as direct microscopy negative (DM-) if microorganisms cannot be found. Other diseases such as bronchiectasia, chronic bronchitis, emphysema, cardiac disease etc. must be excluded.

- *Extra-pulmonary TB*
  All other types of secondary TB, for example:
  - *TB-lymphadenitis*
  - *TB-pleuritis*
  - *TB meningitis*
  - *TB pericarditis*
  - *uro-genital TB*
  - *TB-peritonitis*
  - *miliary TB : Common symptoms are fever and wasting; this may be associated with cough, lymphadenopathy and splenomegaly. The clinical picture is similar to that of typhoid fever or malaria*

CASE DETECTION AND FINDING; DIAGNOSIS

In operational TB management it is important to know, when TB can be suspected. Some of the following symptoms are likely to be present:

TB-symptoms:

- *Persistent cough for three weeks or more; every patient presenting to a health facility with this symptom should be designated a "TB suspect".*
- *Sputum production, which may be blood-stained (haemoptysis) or yellow and purulent if secondarily infected, shortness of breath, chest pain.*
- *Fatigue (tiredness), loss of appetite and weight, general feeling of illness, night sweats and fever, especially in the mornings*
- *Persistent lymphadenitis*

A patient presenting with these symptoms who is, or was, in contact with a person with infectious TB is more likely to be suffering from PTB his/herself.

Symptoms of Extra-PTB depend on the organ involved. Chest pain from TB pleuritis and enlarged lymph nodes and radiologically sharp angular deformity of the spine are the most frequent signs of Extra-PTB.

WHERE IS TB TO BE FOUND?

TB cases are most commonly found in the following circumstances:

- *Among patients, who present on their own initiative at a health facility with symptoms suggesting TB*
- *Among those living in the same household with DM+ patients (especially children and young adults)*
- *Among those, who live under overcrowded and/or poorly ventilated conditions*
- *In those with an abnormality on a chest X-ray, which has the appearance of TB*
- *In all circumstances, where health care providers and community members are aware, educated and involved with a community TB control program. A high index of suspicion is necessary when confronted with symptoms suggesting TB.*

DIAGNOSIS OF TB

Sputum Investigation:

The first and most important diagnostic step is the investigation of the patients' sputum, termed direct microscopy (DM) of the sputum smear.

In all instances, individuals identified as potential TB patients must have an examination of their sputum prior to the commencement of treatment in order to determine whether or not they have infectious TB. This consists of microscopic examination of a specimen of sputum, which has been spread on a slide and stained by the Ziehl-Neelsen method. If TB microorganisms are detected by this method, then the patient is said to suffer from *smear positive (DM+) TB*. Note that this is the only method that allows for a diagnosis of TB in many hospitals in developing countries.

Whenever TB is suspected, *three specimens must be collected for examination*. They should be obtained within 24 hours.

Sputum Culture and Sensitivity

Culture positive, smear negative individuals contribute little to the transmission of TB, provided they are treated at once. Sputum culture should be reserved for smear negative persons and for patients suspected of harbouring resistant organisms in order to conduct sensitivity testing.

X-ray

The diagnosis of TB by means of radiographic examination is unreliable. Mass X-ray screening is not indicated except in abnormal situations where such a screening procedure may be conducted in a timely and geographically restricted area in order to help assess the magnitude of TB as a public health problem.

Abnormalities identified on a chest X-ray may be due to TB, but may also be secondary to a variety of other conditions. Some individuals, who were previously infected with TB that is healed and does not treatment may have X-ray findings that appear like TB requiring treatment. The request to perform X-rays must be made by competent health staff.

TB Skin Test

Tuberculin skin testing has limited value in clinical work, especially where TB is common. A positive test is infrequently followed by disease, and a negative test does not exclude TB. Skin testing has limited diagnostic value in adults, but is useful for children, who have been in contact with an infectious case and who are suspected of having TB.

The *TINE-TEST* is usually used for screening purposes and for contact tracing purposes among children less than 16 years old, whereas the *MANTOUX TEST* is preferred for diagnosis.

Other Diagnostic Procedures

In some cases it might be necessary to confirm the diagnosis through *gastric lavage*, especially in children, who have difficulty producing sputum.

The erythrocyte sedimentation rate (ESR) can be used as an additional, and simple, diagnostic procedure in case of DM- PTB. In most cases of TB it will be accelerated.

TB DIAGNOSIS IN CHILDREN

Diagnosis of TB in children is quite difficult. The distinction between possible and probable TB must be considered.

TB appears most commonly as uncomplicated PTB, as disseminated TB, TB meningitis, spinal TB and in is found in immunosupressed children. All children with TB should be treated to prevent complications and to ensure that they will not subsequently reactivate their infection. Only a very small proportion of children have TB that is smear positive. Many children cannot produce sputum.

Important aspects of the diagnostic process are:

- *History of contact with a case of infectious TB, particularly in the same household*
- *An abnormal chest X-ray showing unilateral lymphadenopathy and/or shadows in the lung field indicating infiltration*
- *A positive skin test (TINE or MANTOUX)*

In the absence of all the above, it is unlikely that the child has TB. Any child, whose skin test remains consistently negative over several months of observation and whose clinical condition is good or shows improvement, does not have TB. Any child under six years of age with a positive skin test, who has not been vaccinated with BCG (Bacillus Calmette-Guerin), but who has signs or symptoms suggesting TB, should be regarded as having active TB and be given short course chemotherapy (SCC).

To clarify the problems with diagnosis of childhood TB, the WHO recommends the following criteria to classify TB cases as suspect, probable and confirmed.

Suspected Tuberculosis

- *An ill child with a history of contact with a suspect or confirmed case of pulmonary tuberculosis*
- *Any child who does not return to normal health after measles or whooping cough*
- *Symptoms such as loss of weight, cough and wheeze which are not responsive to antibiotic therapy for acute respiratory disease*
- *Symptoms such as abdominal swelling, or a hard painless mass and free fluid*
- *Symptoms such as painless firm or soft swelling in a group of superficial lymph nodes*
- *Symptoms such as bone, or a joint lesion, of slow onset*
- *Signs suggesting meningitis or a disease in the central nervous system*

Probable Tuberculosis

- *Suspected tuberculosis and any one of the following:*
- *Positive > 10 mm induration tuberculin reaction*
- *Suggestive radiological appearances on films of chest, bones or joints*
- *Suggestive histological findings in biopsy material*
- *Favourable response to specific anti-tuberculosis therapy*

Confirmed Tuberculosis

- *Probable case and*
- *The detection by direct microscopy or culture of tubercle bacilli from secretions or tissue, or*
- *The identification of the tubercle bacilli as Mycobacterium tuberculosis by culture.*

COMPLICATIONS OF TB

Complications of Pulmonary TB

- *Haemoptysis – coughing up blood*
  all cases should be referred to the next hospital, blood to be inspected by trained health staff.
- *Acute respiratory distress*
  1) due to pneumothorax, collapse of the lung, caused by TB damage
  2) due to pleural effusion: fluid in the thorax, which may need prompt relief by aspiration
  3) due to cardio-pulmonary insufficiency secondary to heart and lung disease as a result of cor pulmonale (right heart failure)
- *Bronchiectasis, fibrosis of the lungs*
  these are consequences of extensive TB associated with persistent purulent sputum. Such patients require hospital care in most instances.
- *Complications of Extra-pulmonary TB*
  Complications of Extra-PTB depend on the organs involved. Extra-PTB is not a major problem in developing countries, and account for less than 15% of all TB cases.

All of these complications need urgent attention and hospital care!

TB TREATMENT AND PATIENT MANAGEMENT

The basic treatment of TB is chemotherapy. With it, virtually all patients can be cured. It is also the only medical means to prevent the spread of TB microorganisms.
The requirements for adequate and effective chemotherapy are:

- *An appropriate combination of anti-tuberculosis medication to prevent the development of resistance to these medications*
- *The combination must be prescribed in the correct dosage*
- *It must be taken regularly by the patient*
- *It must be taken for a sufficient period of time to prevent relapse of the disease after cure.*

Treatment must be given to every patient confirmed as having TB and it must be given *free of charge*. Treatment must always be started as soon as possible after receiving a smear positive laboratory report, or after two sputa have been submitted on a patient who is clearly clinically ill with a high suspicion of TB.

The successful treatment of the patient requires that they understand what is happening. If the patient understands the nature of the disease and its treatment, this information can be disseminated by them to their community which may cause other individuals with suspect TB to come forward to seek diagnosis and treatment.

The patient should have a clear understanding of the following questions:

- *What is TB?*
- *How is it spread?*
- *What measures can be taken to limit its spread?*
- *How is it treated?*
- *Can TB be cured?*
- *What medication must I take and for how long?*

The most common treatment error occurs when health workers trust that their patients will take all their anti-TB medicines regularly and for the prescribed duration. In reality, patients frequently forget to take their medicines or stop taking them once they start feeling better, or they may stop treatment because of severe side-effects.Patients may take only one of their medications avoiding others because they are more difficult to swallow, seem more likely to upset their stomach or simply look less appealing.

From a public health perspective, one of the worst things that can happen during the course of TB treatment is that the patient is not cured. If patients are not cured, the only thing that is accomplished is to make them well enough, and contagious, when they return to their communities to infect others. **TB patients must not only be treated – they must be treated and cured**. During this period TB patients and their families need adequate and sufficient symptom control and care.

BCG VACCINATION AND CHEMOPROPHYLAXIS

BCG *vaccination* is the best way to prevent serious forms of TB in childhood. BCG reduces the risk of getting clinical TB by approximately fifty percent, but the efficacy drops rapidly beyond infancy. BCG vaccination gives a good protection against miliary TB and TB meningitis (6, 7).

The vaccine is injected intradermaly on the upper left arm at a dose of 0,05 ml for infants up to the age of one year and 0,1 ml for children older than one year. The goal for BCG coverage should be 100%.

Chemoprophylaxis is a means to treat people who are at risk of developing the disease if they remain untreated. Isoniacid (INH) is usually given as prophylactic medication.
It should be given for six months and must be considered for persons showing the following picture:

- *Contact to persistent smear positive TB patients*
- *Infants born to smear positive mothers*
- *Children under six years of age, who come into contact with smear positive adults, show a positive skin test but have no clinical or radiological signs of active TB.*
- *High risk patients with, e.g., HIV*
- *Diabetes mellitus*
- *Long-term steroid therapy*
- *Leukaemia*
- *Other chronic malignant illnesses*
- *Alcohol abuse*

DIRECTLY OBSERVED TREATMENT, SHORT COURSE (DOTS)

The strategy that has proven most effective in curing TB patients is called directly observed treatment, short course (DOTS). The DOTS strategy uses a combination of four different drugs to kill the TB bacteria within a six to eight month treatment period. As part of the DOTS strategy, health workers counsel and observe their patients swallowing each dose of medicine while the health services monitor the patients' progress until they are cured. No other TB control strategy has consistently demonstrated such high cure rates of TB patients. DOTS produces cure rates as high as 95 percent, even in the poorest of countries. Other TB programmes, which are not using DOTS may cure no more than 40 percent of their patients. A six-month supply of medicines for DOTS costs only $11 per patient in some parts of the world [8]. The World Bank has ranked the DOTS strategy and BCG immunisation in countries with high risk of infection as some of the "most effective of all health interventions" [9]. Studies in India and Thailand have shown that a small investment in the DOTS strategy can save their economies milliards of US dollars.

DOTS does not require hospitalisation, a high-tech technology or a new health care structure. Rather it utilizes and improves the efficiency of the existing community-based primary health care system. Using the DOTS treatment strategy is simple and effective and offers excellent prospects for improving the quality of life and life expectancy for people living with HIV (see Tables 1, page 191 and 2, page 192).

The five anti-TB drugs currently used for SCC are:

- *Isoniazid*
- *Rifampicin*
- *Pyrazinamide*
- *Ethambutol*
- *Streptomycin*

MAJOR SIDE EFFECTS OF ANTI-TB MEDICATION

These are the side effects that require the medications to be stopped and frequently the patient to be hospitalized for management.

Generalized Reactions

Rifampicin, Pyrazinamide and **Streptomycin** can cause shock, purpura, blistering and fever. The medication that is found to be responsible for the reaction should then be stopped and might be reintroduced singly at 2 day intervals under supervision, or alternatively never be given again.
Visual Impairment reactions may be due to Ethambutol. Patients experiencing this symptom should report immediately for visual examination. If Ethambutol is thought to be responsible, it should never be given again.

Hepatitis

Is present when the patient develops jaundice. It is mostly commonly due to **Isoniazid**, but may also be caused by **Rifampicin** and **Pyrazinamide**. Treatment should be stopped, until the liver function normalizes.

Dizziness, Tinnitus, Vertigo

May be caused by vestibular damage due to **Streptomycin**. These symptoms are most common in older individuals and children. Streptomycin should never be given to pregnant women, because of its side effects on the unborn children.

Neurological Signs

May be due to **Isoniazid**. Vitamin B complex should be given and the medication may have to be stopped.

Table 1. Drugs and dosages for newly diagnosed cases of TB

Drug	Daily dosage	No. of tabs/day	Duration Treatment / Re-Treatment
Adults < 50 kg			
Isoniazid	300 mg/d	1 (300 mg)	6 Months
Rifampicin	450 mg/d	1 (450 mg)	2 Months
Pyrazinamide	1,5 g/d	3 (500 mg)	2 Months
Ethambutol	800 mg/d	2 (400 mg)	6Months
Streptomycin	750 mg/d/imi **	1 vial imi **	2 Months
Adults > 50 kg			
Isoniazid	300 mg/d	1 (300 mg)	6 Months
Rifampicin	600 mg/d	2 (450mg + 150 mg)	6 Months
Pyrazinamide	2 g/d	4 (500 mg)	2 Months
Ethambutol	1,2 g/d	3 (400 mg)	2 Months / 6 Months
Streptomycin **	1 g/d/imi	1 vial imi	2 Months
Children > 6 years			
Isoniazid	10 mg/kg/d		6 Months
Rifampicin	10 mg/kg/d		6 Months
Pyrazinamide	35 mg/kg/d		2 Months
Ethambutol	15 mg/kg/d		2 Months
Children < 6 years			
Isoniazid	10 mg/kg/d		6 Months
Rifampicin	10 mg/kg/d		6 Months
Pyrazinamide	35 mg/kg/d		2 Months

** Only in case of re-treatment

MULTI-DRUG-RESISTANT TUBERCULOSIS

The emergence of strains of TB that are resistant to two or more drugs used for treatment is threatening to make the disease as incurable as it was before the discovery of antibiotics in the 1940s. Unfortunately, improper administration of anti-TB drugs and bad management by TB control

programmes are the primary causes of the spread of drug-resistant tuberculosis. It is estimated that about 50 million people are already infected with a multi-drug-resistant form of TB.

Multi-drug-resistant TB can only develop in humans. It develops when doctors or other health care workers prescribe the wrong drugs or the wrong combination of drugs. Above all, drug resistance occurs if the correct anti-TB drugs are not taken regularly or are not taken for the entire six months of treatment. Health care workers must ensure that TB drugs are taken correctly. Treatment of TB requires supervision. If a patient develops drug-resistant TB, treatment options are severely limited and such a case becomes incurable in developing countries. Every time a patient is incompletely cured, the surviving bacteria may become resistant to the drugs that were used in the treatment. Ultimately a patient can have a strain of TB that is resistant to the most powerful drugs used in the treatment of tuberculosis.

"Poorly supervised and incomplete TB treatment is actually worse than no treatment at all" [2].

Table 2 - Treatment of TB meningitis

Drugs	Daily dosage	Duration
Isoniazid	15 mg/kg	6-12 months
Rifampicin	20mg/kg	6 –12 months
Pyrazinamide	35 mg/kg	2 months
Ethambutol	20 mg/kg	2 months

PATIENT MANAGEMENT

Good patient management is essential for TB control. In principle, the TB Control Programme regards the TB patient as an out-patient. Admission to a health facility should only be reserved for severe or complicated cases. Admission might not be necessary if the patient is well, compliant and living near a health facility.

Hospitalization must be seriously considered if the patient shows one or more of the following:

- *Non-compliance*
- *Persistent smear positive tests*
- *Multi-drug-resistance*
- *Signs of serious illness and TB complications*
- *Severe social problems*
- *Malnutrition, alcohol abuse*

The treatment phases are divided into two components:

I. Intensive phase

II. Continuation phase

The intensive phase of treatment covers the first two months of treatment. During this time, and

beyond, the patient should receive Directly Observed Therapy (DOT) and, of course, adequate symptom control. A sputum smear investigation is done at the end of the second month of treatment and will in most cases show sputum smear conversion to negative.

The continuation phase starts with the third month of TB treatment when a patient who was smear positive becomes smear negative. The continuation phase is combined with *social and physical rehabilitation* of the patient. It is during this phase of treatment that patients are in most danger of defaulting on their medication regimen. Prevention of default is of paramount importance. Sufficient care and symptom control may counteract to this development.

SOCIAL PREVENTION AND REHABILITATION

TB in general is a disease of the impoverished and its underlying causes are all closely interrelated and listed below:

- *Poor socio-economic conditions, unemployment*
- *Overcrowding*
- *Poor ventilation*
- *Illiteracy, lack of health awareness and health education*
- *Insufficient nutrition and hygiene*
- *Poor general health status and alcohol abuse*

It is beyond the control of health workers alone to improve all the underlying causes; therefore collaboration with family and relatives is needed. Awareness must be promoted for those at risk. Simple changes requiring little input must be encouraged, for example improvement in ventilation and hygiene. Education to promote patient and family compliance should be tried particularly in developing countries. Improvisation is important. Only if people understand the interrelation between their living conditions and TB, are they likely to look for changes that are positive.

Rehabilitation measures are very important for many TB patients, as the disease can cause major impairments both emotionally and physically. Rehabilitation means "return to ability", i.e. persons with physical, social, vocational and/or economic problems receive an opportunity to return to the fullest activity possible.

The family and employer need to be informed that in most cases the patient will be non-infectious and able to resume work after at least two months of treatment, often sooner. Health workers should foster an environment where TB patients are not excluded from social life, fall into isolation, dependency or even shame.

NUTRITION

Special attention needs to be given to the nutrition of TB patients, as well as people at risk of contracting the disease. For example, alcohol abuse in parents in conjunction with limited income for buying food, and neglect of optimal breastfeeding children are contributing factors to malnutrition. TB patients require a

balanced diet composed of foods that are affordable. It is a well-known fact, that in urban areas where health care facilities offer one free meal/day as an incentive for patients to participate and also be observed to take their medication, there is less likely to be an interruption of the treatment program.

Other things to do:

- *The health worker must educate TB patients and their families about the importance of good nutrition during treatment and as a preventative measure.*
- *Patients should be informed that alcohol not only weakens the body, but also suppresses appetite.*
- *Patients must be discouraged from smoking in order to prevent lung infections.*
- *Mothers should be encouraged to breastfeed their children for at least six months after birth.*
- *Garden projects, either at clinics or in the community, should be promoted. They create income and produce needed food.*

SYMPTOM MANAGEMENT

As mentioned before, TB is curable in the majority of cases. However, many patients still die of TB due to the presence of concomitant incurable conditions such as HIV, development of resistance to antimicrobial drugs, and lack of compliance or access to the curative treatment. Palliative care in these cases is particularly important.

The focus of palliative care is to provide excellent medical as well as physical, psychosocial and spiritual support to patients and their families who are affected by a progressive incurable illness. Patients with incurable TB may present with many symptoms that can be controlled, such as, pain, dyspnea, cough, haemoptysis, weakness, cachexia and fatigue. Table 3, page 195, summarizes the main symptoms in patients with advanced tuberculosis.

Cough

Dry cough is almost always present in patients with tuberculosis. As the disease progresses it frequently results in the production of bloody sputum, or hemoptysis. A number of opioid-based antitussives and opioid analgesics such as morphine can reduce the cough reflex. Inhaled cromoglycate can prevent cough crisis in patients with malignancy and it may also be tried in patients with cough related to tuberculosis.

Hemoptysis

Using red towels, dark sheets and basins for collection of the blood can comfort patients with severe hemoptysis. The dark color makes the blood less visible thus making it less stressful for both the patient and the family. If a patient has a high risk of bleeding or choking to death secondary to hemoptysis it is useful to have available in the home, a preloaded syringe containing a short-acting benzodiazepines, such as midazolam, or lorazepam. The family should be educated about the possibility of massive bleeding and instructed on how to administer a tranquilizing injection when needed to reduce the patients distress.

Table 3 – Main Symptoms in Advanced TB	
Symptom	**Recommendations**
Dyspnea	An open window or fan stimulate the sensory nerves in the face and nasopharynx Opioids Oxygen may be helpful in patients with hypoxemia
Fatigue and Cachexia	Psychostimulants and antidepressants Blood transfusion if anemia is present Thalidomide Food intake alone is unlikely to resolve severe weight loss
Dry Cough and Hemoptysis	Opioid antitussives Inhaled cromoglycate Have red towels available and dark sheets and a basin to collect the blood In case of massive bleeding or chocking, use short acting benzodiazepines (midazolam or lorazepam)
Pain	Opioids, NSAIDS
Fever	Acetaminophen, NSAIDs
Night Sweats	Acetaminophen, NSAIDs

Dyspnea

Supplemental oxygen may be helpful particularly in patients who have hypoxemia. Air provided by a fan or simply an open window can reduce the intensity of dyspnea by stimulating the sensory nerves at the face and nasopharynx.

The most effective drugs for the management of dyspnea are opioid analgesics such as morphine. Appropriate doses of an opioid are capable of reducing the intensity of dyspnea without significantly reducing the respiratory rate. Patients treated with opioids will experience less dyspnea while still breathing fast. This information should be shared with the families since it is common that relatives may interpret tachypnea as a sign of dyspnea.
Benzodiazepines are occasionally useful for reducing severe anxiety in patients with dsypnea.

Fatigue and Cachexia

This is one of the most common and severe problems in patients with tuberculosis. It is also important to manage the symptoms of pain, depression in addition to fatigue and cachexia.

Psychostimulants and antidepressants may be helpful in the management of subjective symptoms of fatigue.

Patients with anemia may benefit from blood transfusions when available.

Thalidomide can occasionally be helpful in the management of fatigue and cachexia in patients with tuberculosis, HIV and cancer.

Unfortunately, increased food intake alone is unlikely to resolve the severe weight loss related to tuberculosis since cachexia is a syndrome resulting from metabolic abnormalities. Cachexia related to tuberculosis, HIV, and cancer does not the result of a simple caloric imbalance and is seldom reversed with aggressive nutrition including total parenteral or enteral nutrition. It is very important to maintain the social value of meals even when patients have minimal intake. Provide families with the information that patients are not starving to death, but rather experiencing the expected metabolic consequences of advanced tuberculosis.

Night Sweats

This is a common and unpleasant symptom at the beginning of the illness. The appropriate management of fever can help and it is important that patients maintain adequate hydration.

Pain

Thoracic and bone pain are common and usually easily controlled with traditional treatment with opioids and non-steroidal anti-inflammatory agents.

THE NAMIBIAN TB-REHABILITATION MODEL PROJECT

Between 1995-2002, a German non-government organisation (NGO) which is involved in the German health service and committed to work in several African countries, carried out a project to fight the rapid increase in the number of tuberculosis cases in Namibia. The project's aim was to assist local medical personnel to adopt a plan of action for autonomous health care administration regarding tuberculosis. The plan was to provide for an extensive fight against tuberculosis even with their extremely modest means, and to eliminate compliance problems by using regular medication intake supervision.

The first TB-Rehabilitation Centre was established in Katutura in 1996 with minor financial support from Germany.

During the initial phase of treatment, patients were placed under Directly Observed Therapy, Short Course (DOTS). DOTS succeeds for one pivotal reason: It makes the health system – not the patient – responsible for the success of a curative treatment. This is critical, as most TB patients when they begin to feel better, after just a few weeks into treatment, often are tempted to discontinue therapy. Poor patient compliance due to a high rate of side effects was the biggest challenge. In most instances, continued TB-treatment is without risk to the patient.

Symptomatic treatment and reassurance of the patients may be sufficient for minor or major side effects. Isoniazid and Rifambicin cause skin reactions, Pyrazinamide causes joint symptoms, and Rifampicin causes a flu-like illness and/or abdominal pain, nausea and vomiting. Other side effects of Rifampicin include a red/orange colour of body fluids (tears, saliva, sputum and sweat) that is not dangerous, but patients should be informed that it may occur. The most common reaction of patients who experienced one or more of the above-mentioned side effects was to become non-compliant or default on treatment. One of challenges of the project was to increase patient compliance by

prophylactically minimizing side effects, if possible, or by aggressively treating them when they occur. Providing one meal/day at the time of observed anti-TB drug indigestion proved a most effective, simple and cost-effective solution. Two weeks after beginning the initial phase of the model project, more than fifty TB patients were waiting for breakfast at 7 a.m. Most of them reported that they stopped losing weight and felt better since taking anti-TB drugs. Prior to the beginning of the project, patients would spit out the drug and attempted to sell them to other patients, this did not happen after the project was begun.

Patients were motivated to come to the clinic each day by providing a warm meal. This strategy was called "therapy with a goulash gun". As part of this program, patients were encouraged to participate in light work such as keeping vegetable gardens around the centres that later were used for their nutrition. This mild exercise had beneficial metabolic effects and major psychological benefits for patients and families. Patients who became well enough to return to their communities served as multipliers of this method within their community and thus enhanced the compliance of neighbours who were also infected with TB. Six centers in Katutura and one in Rundu in north Namibia were established by 2002.

Other specific programs like HIV-prevention, family planning, health and body care, traditional crafts, child care, horticulture, hospice and palliative care and spiritual counselling were offered on a daily basis.

The family members of TB patients, their relatives, potential caretakers and other community members close to the patient need to be involved in all rehabilitation measures. The same applies to employers, who need to know about TB as a disease, rehabilitation possibilities and what needs to be done to rehabilitate an employee. There is no need for any retrenchment, if TB is diagnosed early enough and patient management is according to the treatment guidelines.

Many vegetable gardens around the centers are harvested three or four times a year. More than 60% of all food needed comes from these gardens. The remaining expenses for food and plants, about US$10,000 annually, are covered by sponsors in Germany.

In 2001, the success rate for the treatment of TB in Namibia reached 70% (50% in 1996) and the incidence of multi-drug resistance was below 5% [10].

Highly successful programmes for the control of tuberculosis were achieved in Namibia by coordinating directly observed therapy of anti-TB drugs with the provision of food to the patient and family, mostly children. This improved compliance and the quality of life of the patient and his/her family and also reduced the gastrointestinal side effects of anti-TB drugs by allowing patients to take medications with their meals.

CONCLUSION

Tuberculosis is one of the most pressing public health problems worldwide. After a steady decline until the mid-1980s, the number of TB cases rose again with the advent of the HIV/AIDS epidemic. Today, TB affects, and kills, more people than any other infectious disease. Once identified, TB can be effectively treated and rapidly can become non-infectious. TB can be cured in 95% of all cases, including patients infected with HIV. However, careless and chaotic treatments of tuberculosis are spawning a TB bacteria that are resistant to previously effective anti-TB drugs. Excellent patient management and sufficient symptom control are essential for TB control. Health care workers must ensure that powerful TB drugs are taken correctly. One of the worst things that can happen during the course treatment of TB is that a patient is treated, but not cured. Directly Observed Treatment, Short Course (DOTS) is a comprehensive strategy that primary health services around the world are beginning to use to detect and cure TB patients. As part of the DOTS strategy, health workers counsel and observe TB patients swallow each dose of anti-TB medicines until they are cured.

In the case of Namibia, highly successful programmes for the control of tuberculosis were achieved by coordinating directly observed therapy with anti-TB drugs and the provision of food ("therapy with a goulash gun") to patients and families. As part of the same programme, patients were encouraged to participate in light work such as keeping vegetable gardens around centres from which the produce is used for their nutrition.

The only way to prevent the increasing problems associated with TB in developing countries is to aggressively find solutions that are easy to implement in countries where there are limited resources and poor infrastructure. One such program is the directly observed medication treatment program described in this chapter. There is great need for change in dealing with this health problem because the fight against tuberculosis is also a fight against time. A major emphasis of the treatment of TB must also include palliation and effective symptom management.

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12 Malaria

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Malaria has been one of the most prevalent human diseases in tropical regions of the world. It is mentioned in early writings from Egypt, India and China, and is currently responsible for more than 300-500 million acute illnesses and 1-2 million deaths per year. Malaria is a parasitic disease caused by the genus *Plasmodium*, which is transmitted to humans through the bite of female mosquitoes from the genus *Anopheles*. It manifests with flu-like symptoms, severe cyclic fevers, sweating spells and anemia. The disease undermines the health and welfare of families, debilitates the active population, and strains the country's scarce resources. Children and pregnant women are most vulnerable, for malaria is an important cause of maternal anemia, low birth weight and perinatal mortality. This disease is distributed in more than 90 countries, most located in tropical areas of Africa, Asia and Latin America. This geographical distribution sadly coincides with what some call "the belt of poverty" which expands around the globe through the Equator.

MORBIDITY AND MORTALITY

Forty percent of the world's population is at risk of attaining the disease, and ten percent will have an acute attack per year. However, as cited in chapter 3 *only one sixth of 1% of global Research and Development (R&D) resources in biomedical research are devoted to malaria largely because most malaria victims are impoverished and therefore ignored by private industry*. It has been calculated that 76% more productive life years are lost from malaria than from all cancers in developed countries, and still funding for cancer research can be 10 to 50 fold greater.

Although malaria is a curable disease, fatalities due to this entity correspond to 2% of the total mortality worldwide, which is one tenth of the total mortalities due to infectious diseases. More than 90% of malaria cases and the majority of deaths due to malaria occur in Sub Saharan Africa. One African child dies from malaria every 30 seconds, and survivors frequently have cognitive and developmental impairment as sequelae from severe malaria suffered in childhood. Efforts are being made to detect the underlying reasons for malaria's capacity to become a life threatening disease. Greenwood, Marsh and Snow describe the phenomenon as an interaction of factors such as: the amount of infective sporozoites, level of acquired immunity, presence of sickle cell hemoglobin, nutritional status of the host and availability of health care and education. It is clear that there is a

strong social component contributing to morbidity and mortality from malaria. While we are still trying to elucidate the microbiological causes of severe disease, social causes of chronic debilitating illness and mortality are the direct responsibility of governments, health care professionals and the community as a whole. Implementation of prevention strategies, education, and availability of adequate treatment are our responsibility. Efforts from international entities, such as the "Roll Back Malaria" program from the World Health Organization (WHO), United Nations Children Fund (UNICEF), United Nations Drug Control Program (UNDP) and the World Bank, aim to diminish the burden of malaria by 50% in a 10 year period (2000-2010). These global efforts do not create immediate solutions, as is expected, since they are part of a long process and we are far from eradicating the disease. It is thus important for doctors and people living in, or traveling to, endemic areas to be well informed about the clinical manifestations of the disease in order to obtain adequate and prompt therapy. Meanwhile, we still have to deal with cases of severe malaria, with multi-organ disorder. Palliative care for control of seizures, fever and pain may be the best we have to offer in some cases.

ETIOLOGY

Malaria is a mosquito-borne infection caused by four species of obligate intracellular protozoa from the genus *Plasmodium: P.falciparum, P.vivax, P.ovale and P.malariae. P.vivax* is the most widely distributed while *P.falciparum* is the most pathogenic. Presence of these species varies from country to country. *P.falciparum* is distributed in the tropics and subtropics, particularly in Sub Saharan Africa, where it is responsible for more than 80% of malaria cases; hence this region contributes the most malaria fatalities. *P.vivax* as said before is widely distributed, mainly in Latin America and Asia, and is responsible for most malaria cases diagnosed in the United States. It causes mild recurrent disease if the first episode is not treated appropriately. *P.ovale* is rare, found mainly in West Africa, Southeast Asia, New Guinea and the Philippines, and it can also cause recurrent disease. Finally, *P.malariae* has a variable and spotty distribution, mainly in Africa. It can live in asymptomatic hosts for decades or it can manifest as an acute illness. It has been associated with membranoproliferative glomerulonephritis and nephrotic syndrome in children.

Plasmodium is transmitted to humans through the bite of a female anopheline mosquito that feeds at night time. The infective form, "sporozoite" reaches the blood stream and then travels to the liver, where it infects hepatocytes and multiplies within a form called "squizont", which contains thousands of "merozoites". After a 6-16 day period merozoites are liberated into the blood stream. Up to this point we have described what is called the exoerythrocytic phase of infection, which is asymptomatic. In the second, "erythrocytic" phase, merozoites invade red blood cells (RBC). Once inside RBCs they turn into ring forms called "trophozoites" that degrade hemoglobin. Once more, within the RBC the parasite forms squizonts, multiplies and liberates thousands of merozoites into the bloodstream that will infect new RBCs. This process continues in repetitive cycles of erythrocyte invasion and lysis, with hemolytic anemia as a result. Some merozoites, however, differentiate into "gametocytes", which is the form acquired by female mosquitoes after biting an infected human host. The parasite completes its sexual cycle in the invertebrate vector, where new sporozoites are formed and are ready to infect another human host. Finally, P.vivax and P.ovale, have the capacity to remain dormant in liver parenchyma cells for periods of months to years; these forms of latent parasites are called "hypnozoites" and are responsible for recurrent episodes of malaria if specific treatment is not administered.

CLINICAL MANIFESTATIONS

Malaria can be viewed as a spectrum of clinical entities that include: asymptomatic parasitemia, acute febrile illness, and severe malaria that can lead to mortality. The most common form of malaria is an acute febrile illness characterized by general malaise, headache, backache, vomiting, anorexia, chills, fevers, and sweating spells (malarial paroxysm). Anemia, jaundice, splenomegaly and hepatomegalia follow. The fevers are classically described as cyclic: every two days "tertiary" for *P.vivax, P.ovale* and *P.falciparum,* and every three days "quaternary" for *P.malariae.* The difference in patterns of fever comes from the different times at which merozoites of different species are freed from RBCs. After lysis of RBCs, digested hemoglobin, toxins and parasite antigens are liberated into the bloodstream and elicit an immune reaction that causes the symptoms described above. Frequently, *P.falciparum* malaria does not present with such cyclic patterns of fever, for RBCs are infected in several stages and thus the continuous rupture of these cells is responsible for symptoms between these "cycles".

For purposes of this book we will focus our discussion on manifestations and treatment of severe malaria, and in particular cerebral malaria, caused by *P.falciparum.* This species has the unique capacity to infect RBCs of all ages, and thus produce high-grade parasitemia and obstruction of microvasculature that can lead to complicated malaria with compromise of multiple organ systems.

DIAGNOSIS

Malaria can be mistaken for a number of acute febrile illnesses. It is therefore crucial for the clinician to have a high grade of suspicion in order to look for it and treat it appropriately. It should always be considered in the differential diagnosis of acute febrile illnesses in endemic areas, or in people with a travel history to these areas. The incubation period of the parasite, which ranges from 8 days to 24 days, except for *P.malariae*, with a longer incubation period that ranges from 18 to 42 days, is used to determine if there is a chronological link between exposure and clinical manifestations. Furthermore, malaria should be considered in patients from endemic areas with history of blood transfusions. In this case symptoms are expected to appear 48 hours after the transfusion. History of previous malaria infections or travel to endemic areas, even months before, should be considered as possible causes of recurrent malaria or of long standing infection with atypical manifestations due to inappropriate prophylaxis.

Fortunately the gold standard laboratory test for malaria diagnosis, the thick droplet test, is highly sensitive, specific, and does not require expensive equipment or facilities. It is thus an economic, minimally invasive procedure available throughout the world. Blood is obtained through a finger prick. Thick and thin blood smears are prepared and visualized under the microscope for presence of parasites. The thin smear permits more adequate visualization of parasite morphology and thus the identification of *Plasmodium* by species. This information is used to select the adequate therapy for the infecting species. Rapid diagnostic tests (RDT) have been introduced recently. These tests detect parasite antigens by immunochromatography. Although RDT are easier to perform and interpret, and can provide results in about 15 minutes, their sensitivity varies among species and decreases markedly in cases with less than 100 parasites/mL. False positives have also been reported.

DIFFERENTIAL DIAGNOSIS

As mentioned above, non-complicated malaria can be confused with a number of acute febrile illnesses. Diagnosis of severe malaria, and particularly cerebral malaria, is a challenge for clinicians due to its rapid evolution and high mortality rate. It is thus crucial to make the diagnosis and initiate treatment sometimes even before laboratory tests are available. Entities that might be considered in the differential diagnosis of cerebral malaria are: meningitis, encephalitis, typhoid encephalopathy, sepsis, stroke, metabolic coma, and eclampsia. It is sometimes difficult to differentiate cerebral malaria from severe infections associated with altered level of consciousness. CSF studies from lumbar puncture, serological studies for viruses and blood cultures for salmonella and other bacteria may exclude or confirm entities with similar presentations. A history of traveling to, or residing in, an endemic area should prompt the clinician to suspect malaria. However in patients taking malaria prophylaxis, suppression of parasite's growth makes microscopic detection difficult. For practical purposes, parenteral antimalarial therapy for cerebral malaria is justified in cases of diminished level of consciousness if history raises any suspicion about malaria. A positive *P.vivax, P.ovale or P.malariae* smear does not exclude the possibility of mixed infection with *P. falcifarum.*

MANAGEMENT

The success of severe malaria management depends upon early detection of the parasite and general supportive measures, anti-malarial therapy, management of complications as they arise and palliative care. (Tables 1 and 2)

TABLE 1. GENERAL SUPPORTIVE MEASURES FOR SEVERE MALARIA

1. *Patients should be treated in an intensive care unit*
2. *In endemic areas, treatment should be commenced as early as possible, sometimes before positive parasitology.*
3. *Patients should be weighed so that the dose of antimalarials can be calculated.*
4. *Intravenous fluids should be given to maintain fluid balance and caloric requirements. A central line and monitoring of central venous pressure may be necessary, especially in the elderly. All intakes should be recorded carefully.*
5. *Urinary catherization should be used to monitor urine output.*
6. *Patients should be observed for vomiting. To ensure patient safety-cot-sides may be required.*
7. *Regular re-positioning of patient is necessary to prevent development of pressure sores.*
8. *Nasogastric tubes should be avoided because of the risk of aspiration.*

Antimalarial Therapy

The most important part of severe malaria management is to save patient's life by rapidly killing the parasite. Due to the widespread presence of choloroquine resistant *P. falcifarum*, chloroquine is of limited value in severe malaria. The WHO recommends a loading dose of quinine (20mg/kg BW) by continuous intravenous infusion for 4 hours followed by 10 mg/kg BW every 8 hours. Various treatment regimens have been tried in the management of severe malaria. (Table 3) The WHO recommended treatment for severe malaria with loading doses of quinine is still associated with high mortality and hopes that artemether would be superior to quinine have not been sustained. Adjuvant therapies such as steroids, dextran, heparin, pentoxyphylline and desferioxamine, have all proved unsuccessful means of improving outcome. Finally, to improve the clinical management of cerebral malaria, there must be a clearer understanding of the pathogenesis.

TABLE 2. BASIC CHEMOTHERAPY PRINCIPLES FOR SEVERE MALARIA

1. *Treatment should begin as soon as possible.*
2. *Dosage should, whenever possible, be calculated according to the patient's weight.*
3. *The parenteral route is preferred to the oral/rectal route.*
4. *Response to treatment should be monitored continuously: clinical assessment, temperature, blood pressure, respiratory rate, malaria parasite smear.*
5. *Treatment should be switched to the oral route as soon as the patient is able to take oral medication.*
6. *Side effects of drugs should be monitored: hypoglycemia, cardiac arrhythmia, blood pressure.*

TABLE 3. RECOMMENED DOSES OF ANTIMALARIAL DRUGS FOR TREATMENT OF SEVERE MALARIA

DRUG	SIDE EFFECT
Quinine: 20 mg of dihydrochloride salt/kg by IV infusion over 4 hours, followed by 10mg/kg over 2 to 8 hours every 8 hours. Patients should not have received quinine or mefloquine within last 24 hours.	Hypoglycemia, cinchonism, tinnitus, hearing impairment, nausea, dysphoria, vomiting, prolonged QT interval dysrrhythmias, hypotension.
Quinidine: 10 base/kg infused at a constant rate over 1 hour followed by 0.02 mg/kg/min, with ECG monitoring. This is used as an alternative drug only, if quinine is not available.	Hypotension, widening QRS complex, prolonged QT interval
Artesunate: 2.4 mg/kg IV or IM initially, followed by 1.2 mg/kg at 12 and 24 hours then 1.2 mg/kg daily	No toxicity documented, reduced reticulocytes, neurotoxiticity in animals, cardiac and gut toxicity in animals.
Artemeter: 3.2 mg/kg IM initially, followed by 1.6 mg/kg daily. Not to be given IV.	
Artemisinin: suppositories, 10mg/kg at 0 and 4 hours followed by 7mg/kg at 24, 36, 48 and 60 hours.	
Chloroquine: 10 mg base/kg infusion at constant rate over 8 hours followed by 15 mg base/kg over 24 hours, or 3.5 base/kg 6 hourly or 2.5 base/kg 4 hourly by IM or SC injection. Total dose 25 mg base/kg	Hypotension

Management of Organ Failure

- *Renal failure: If patient is oliguric (<30cc/h or <400cc/d) initiate EV hydration and standard measures for acute renal failure. May give furosemide and eventually dopamine depending on the patient's response. Electrolyte disturbances (hypo/hyperkalemia, hypo/hypernatremia) should be detected, treated and monitored.*
- *Acidosis: dialysis as soon as possible, bicarbonate only if pH <7.15 pyruvate dehydrogenase activator dichloroacetate.*
- *Hypoglycaemia: administer a bolus of 50 ml 40% dextrose, repeat if necessary, infusion of 10%*

dextrose and monitor blood sugar.

- *Hyperbilirubinaemia: no specific therapy, vitamin K 10mg IV if prothrombin and partial thromboplastin time is prolonged, cholestyramine.*
- *Respiratory Failure: oxygen therapy, mechanical ventilation if necessary.*
- *Hypotension: evaluate volume status, if possible use CVP, IV crystalloid/colloid infusion, dopamine and/or dobutamine.*
- *Sepsis: correct hypotension, check evidence of infection (WBC, differential count, blood culture), broad spectrum antibiotic.*
- *Severe anemia: packed red cell transfusion, if overload is present, diuretic like furosemide should be added.*

Ancillary Treatments

Ancillary treatments are recommended to support anti-malarial drug therapy and reduce mortality. As more information on the pathogenesis of severe malaria is obtained, we will have better ideas for development of adequate ancillary treatments. Some of the ancillary treatments that have been tried and recommendations for use are shown in Table 4.

TABLE 4. ANCILLARY TREATMENTS – RECOMMENDATIONS

Recommended Ancillary Treatment	
Paracetamol for pyrexia	
Phenobarbital to prevent seizures	
Exchange transfusion for hyperparasitaemia > 15%	
Treatments that have shown no benefit in clinical outcome	
Antibody TNF	Prostacyclin
Hyperimmune globulin	Acetylcystein
Dextran	Aspirin
Allopurinol	Corticosteroid
Desferioxamine	Cyclosporine
Pentoxifylline	
Heparin	
Mannitol	

PALLIATIVE CARE

The goal of palliative care is to provide symptom control and psychosocial support to patients and information and psychosocial support to their families. The families need to learn about the nature of the symptoms and their treatments.

Symptom control of patients with severe malaria includes the treatment of fever, delirium, increased muscle tone, management of pain, seizures, and prevention of bedsores.

Delirium

Treatment of delirium depends on the clinical situation. In all cases general supportive measures (quiet environment, reassurance, music) are required. At earlier stages reversible causes (dehydration, hypercalcemia, hypoxia/hypercapnia, drugs, fever, hypo/hyperglycaemia, fecal impaction, urinary retention, etc) must be treated. At advanced stages treatment is symptomatic with neuroleptic drugs: haloperidol (2-15 mg po/sc q6h and 2 mg q1h po/sc PRN) or chlorpromazine (12.5-50 mg po, sc, q4-8 h) or levomepromacine (12.5-50 mg po, sc, q6-8 h) depending on availability. In refractory delirium permanent sedation may become necessary with diazepam (10-20 mg po, im, iv, PRN) or lorazepam (0,5-2 mg po, sl, sc, PRN), or midazolam (25-150 mg/day, sc).

Pain

Patients may experience severe back pain and muscle pain from increased muscle tone. Muscle tone can be reduced with baclofen (5 mg q8h) or/and diazepam (2.5-5 mg q12h). Pain can be easily controlled with the WHO ladder guidelines with non-steroidal anti-inflammatory agents and opioids. Paracetamol (500 mg po q4-6h) or ibuprofen (400 mg po q8h) or naproxen (250-500 po mg q12h) can be used according to availability. For severe pain morphine (5-10 mg q4h, O, SC, IV, and 2,5 mg O, SC, IV q1h PRN) must be used. Drugs should be started at low dosages, and titrated upwards until symptom control or unacceptable side effects occur.

Convulsions (seizures)

The patient should be protected against injury and aspiration during the seizure. A useful approach is to use the benzodiazepine lorazepam (2 mg sc, sl, po q5min) or diazepam (10-20 mg po, im, iv, pr) for rapid control of the convulsion. After seizure control it is necessary for the subsequent administration of an anticonvulsant, the most frequently used are: phenytoin (25-50 mg q12h, po, max. 200-500 mg/day), or carbamazepine (200 mg q8h po; max. 800-2000 mg/day) or Phenobarbital (25-50 mg q6h, sc, po, max. 50-200 mg/day). Which agent is used depends on their availability. Drugs should be started at low dosages, and titrated upwards until symptom control or unacceptable side effects occur.

Bedsores

Bedsores need to be prevented early in bedridden patients. Frequent changes of the patient's position, maintenance of acceptable standard of hygiene and dry and clean bed sheets are necessary. In order to prevent a wet environment capable of precipitating bedsores, it is important to catheterise incontinent patients

Steroids can have a beneficial effect on both the patient's well-being and appetite. The dose of dexamethasone is 8-16 mg (SC) once daily in the morning for 5-6 days; if no clinical benefit is present it can be discontinued abruptly, or the dose can be slowly reduced (2 - 4 mg/day, oral).

The WHO has defined several parameters to recognize cases of severe malaria, these include: coma, repetitive seizures, severe normocytic anemia (hematocrit < 15%), renal failure (creatinine > 3mg/dL), malarial hemoglobinuria, pulmonary edema, circulatory collapse, spontaneous bleeding/CID, hypoglycemia and acidosis. Other supporting features are impaired consciousness, jaundice, prostration, hyperpyrexia and hyperparasitemia (>5% infected RBCs).

Cerebral malaria is the most serious complication of Plasmodium falcifarum malaria and has a high mortality rate. Despite prompt treatment with an effective anti-malarial drug, cerebral malaria has an estimated case fatality rate among hospital admissions of 20-50%. The course of cerebral malaria is very rapid. Studies have shown that on average patients present to the hospital after two days of symptoms, and that most deaths occur within 24 hours of admission. Many factors contribute to this: delay in diagnosis, delay in the initiation of therapy, lack of intensive care facilities, and the fact that patients and their families are often unaware that the condition is serious and warrants hospitalization.

Cerebral malaria is a diffuse rapidly evolving encephalopathy, defined as an unarousable coma of more than 30 minutes after convulsion in a patient with a positive smear for asexual forms of P.falciparum and for whom other causes of encephalopathy have been excluded. More than two convulsions are considered indicative of cerebral malaria. Other features are mild meningism, papilloedema, dysconjugate gaze, vertical nystagmus, 6th nerve palsy, doll's eye and oculovestibular reflex (usually in children). In adults, there is symmetrical upper motor neuron lesion, manifesting as increased muscle tone, brisk tendon reflex, ankle clonus and extensor plantar response. Jaw jerk is sometimes brisk, with presence of pout reflex and absence of abdominal reflex. The cremasteric reflex is preserved.

Another manifestation of severe malaria by P.falciparum is anemia. This phenomenon is the result of hemolysis, RBC sequestration in microvasculature, and decreased erythropoesis secondary to high levels of TNF . Renal failure with tubular necrosis is caused by accumulation of hemoglobin and malaria pigment in renal tubules, and to hypoperfusion due to RBC sequestration and obstruction of renal microvasculature. Inflammatory response from monocytes and neutrophiles causes increased permeability of the alveolar-capillary membrane and consequent pulmonary edema, once more, one of the main factors involved is TNF . Finally, hypoglycemia, is a frequent complication, particularly in pregnant women. Parasitic consumption of glucose, TNF ´s inhibitory effect on liver gluconeogenesis, and hyperinsulinemia induced by quinine are the main causes of hypoglycemia in P.falciparum malaria.

CONCLUSION

Almost half of the world population is at risk of being infected with malaria. This disease diminishes the work capacity of adults and causes developmental and cognitive impairment in children. P.falciparum malaria can cause a severe form of the disease that may lead to multiorgan failure and death. The management of severe malaria requires high clinical suspicion and promptness in therapy, followed by monitoring of clinical response, drug side effects and major organ functions. Palliative care must be offered to patients disabled from cerebral malaria and to those with irreversible multiorgan failure that are prone to die from the disease.

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13 Rabies

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Rabies is a fatal acute encephalomyelitis, which remains one of the most common viral causes of death in developing countries. Previously unvaccinated patients, with rabies have 100% mortality and, without palliation, die agonizing deaths(1). There is very little in the literature on the management of the terminal stages of Rabies especially as applicable in developing countries. The suggestions made here for symptom control outside a well-equipped intensive care setting are from recent work being undertaken at San Lazaro Infectious Diseases Hospital in Manila, Republic of the Philippines.

THE PROBLEM WORLDWIDE

Rabies in humans is a significant problem for developing countries. Reliable data on the incidence of rabies in humans, worldwide are scarce with estimates ranging from 40,000 up to 100,000 cases annually. The size of the problem is reflected in estimates that 10 million people receive post-exposure treatments each year after exposure to rabies suspected animals. Unfortunately the vast majority of people are treated with vaccines that carry a risk of neurological complications.

In developed countries the incidence of human rabies is low e.g. the United States reported 1-2 cases annually in 1990's. Some island nations are reported as rabies free.

The epidemiology of rabies in humans reflects that of local animals rabies. Most human cases in the developed world follow exposure to rabid wild animals e.g. bats, foxes and raccoons, while, in the developing world, e.g. most countries of Africa, Asia and Latin America, bites from domestic and feral animals, usually dogs are responsible.

Transmission between humans has only been documented through corneal transplantation(1, 2)

AETIOLOGY AND PATHOGENESIS

Rabies is caused by a member of the Rhabdoviredae family, a Lyssavirus. This is a negatively stranded RNA bullet shaped virus.

It is transmitted by the introduction of saliva from infected animals i.e. through bites, scratches, licks on broken skin and contact with mucous membranes.

After entry through a skin break or mucous membrane the virus replicates in the muscle cells, infects the muscle spindle and then the nerve innervating the spindle. Further replication occurs within these neurons and the virus spreads centrally towards the central nervous system. Virus is present in dorsal root ganglia within 72 hours of inoculation.

Rabies infection appears to require local viral replication, perhaps to reach a critical load, before nervous system infection occurs. Thus if antirabies immunoglobulin and active immunizations are given in time, virus may be prevented from spread into the nervous system and disease prevented. Once virus has entered the peripheral nerve however, disease is inevitable.

After spreading centrally to the spinal cord the virus spreads throughout the CNS and then centrifugally out to the rest of the body via peripheral nerves.

High concentration of virus in saliva results from viral shedding from sensory nerve endings in the oral mucosa as well as replication in salivary glands(1). The brain in rabies shows an encephalitic picture and the spinal cord severe inflammation and necrosis.

PREVENTION

The control of animal rabies is central to the prevention of human disease. However few countries have been able to achieve this. Thus prophylaxis for domestic animals and humans at high risk and post-exposure treatment for exposed humans remain very important. Dramatic decreases in human cases have been reported recently in China, Thailand, Sri Lanka and Latin America following the implementation of programmes for improved post-exposure treatment of humans and the vaccination of dogs (2). However in most developing countries the cost of these programmes and the cost of controlling feral dog populations remain huge problems and may not achieve political priority.

PRE-EXPOSURE PROPHYLAXIS

- *Pre-exposure prophylaxis (PEP) is usually confined to people with a high risk of rabies exposure e.g. veterinarians and laboratory workers.*
- *Health care workers. Those caring for rabies patients should ideally be vaccinated. Our experience suggests that this is prohibitively expensive and therefore vaccination is unlikely to occur. Thus staff are fearful and may be reluctant to provide even basic physical care for dying rabies patients.*

Note however that transmission to health care workers has NOT been reported and remains more a theoretical risk when normal universal infection control measures are observed. This of course may be very difficult if the patient has uncontrolled aggressive and violent symptoms.

- *Recommended PEP involves vaccination with a series of 3 intramuscular or intradermal injections (on days 0, 7 and 21 or 28) with a booster every 2-3 years(3).*

Post-exposure Treatment

- *First aid:*
  - *Eliminating the virus at the site of infection is the best protection. The wound should be vigorously washed and flushed with soap and water and then ethanol or Iodine or Providone Iodine solution applied.*
- *Anti-rabies immunoglobulin should be give. Either equine (following a skin test) or human immunoglobulin, if available, is used. This is infiltrated in and around the wound. Ideally it is given on Day 0 but may be given up to Day 7.*
- *Vaccination*
  - *This is recommended following a bite from an animal in which rabies is a possibility but may be discontinued if the animal stays healthy for 10 days or is proven at autopsy to be negative for rabies.*
  - *Purified vero cell vaccine (PVCV) or purified duck embryo (PDEV) vaccines are used. Various vaccine schedules are used.*

Two possible schedules are shown in Table 1. WHO Recommendations should be consulted(3).

Table 1: Post-Exposure Vaccination

Reduced multisite intramuscular regime (2-1-1 schedule)	
D0	Both deltoids
D7	One deltoid
D21	One deltoid
D0	Both deltoid regions
D3	Both deltoid regions
D7	Both deltoid regions
D30	One deltoid region
D90	One deltoid region

Obstacles to Treatment

Although such post-exposure treatment may be available, there remain real and heart rending obstacles to obtaining this.

Many patients do not seek help through ignorance, fear, folk beliefs and overwhelming poverty. There are many sad stories of patients being unable to afford the bus fare to present for otherwise free treatment.

Education programmes are making in-roads in some places e.g. San Lazaro Infectious Diseases Hospital treats approximately 60,000 dog bites a year. Encouragingly the number of rabies patients treated there in 2002 was 107 compared to 152 in 2001.

Unfortunately overwhelming poverty and political motivation remain worldwide issues in the eradication of Rabies as with many other global health problems.

Clinical Manifestations

Table 2 shows themain stages of development, the number of days and main symptom in each. Incubation period may be from a few days to several years. The average incubation period is 20-90 days(1).

The time of onset of symptoms depends on;

- *the severity of the wound i.e. the depth, size or multiplicity*
- *clothing protection at the site of bite.*
- *the site of wound in relation to the brain i.e. patients with facial bites develop symptoms earlier*

The early clinical features are:

- *non-specific influenza like symptoms and*
- *localized paraesthesia, pain and pruritus at the bite site.*

The later clinical presentation evolves into two forms:
the encephalitic (furious) form in about 80% of patients or the paralytic (dumb)form..

"Furious" Rabies

The features of encephalitic rabies are typically described as hydrophobia, representing an exaggerated irritant reflex of the respiratory tract with laryngopharyngeal spasm, *episodic hyperactivity, seizures, aerophobia, hyperventilation and autonomic dysfunction* with pupillary dilation, increased salivation, sweating and occasionally priapism.

Paralytic ("Dumb") Rabies

This is characterized by ascending paralysis resembling Guillan-Barre syndrome.

Outcome

Whichever the initial symptom complex, cardiac arrhythmias and coma intervene and death is inevitable within a few days. Most patients die within 72-hours of the onset of clinical features(1).

Table 2		
Stage	**Days**	**Symptoms**
Incubation Periods	<30 days 25% 30-90 days 50% 90 days – 1-year 20% >1-year 5%	
Prodromal and symptoms	2-10 days	Paraesthesia, pain, pruritus at bite site. - Fever, Malaise nausea, vomiting.
Acute disease		
Furious 80%	2-7 days	Hydrophobia Aerophobia Dysphagia Aggression Disorientation Hallucination Anxiety, terror Agitation Hyperexcitability Hypervigilance Confusion Hypersalivation Seizures
Dumb 20%	2-7 days	Ascending Flaccid paralysis

SYMPTOM MANAGEMENT

Delirium

As in any palliative care situation the first priority is good symptom management. This in turn allows personal care of the patient and psychosocial and spiritual issues for the patient and family to be addressed. Previously, rabies patients have died physically restrained, agitated, aggressive, terrified, paranoid and with classic hydrophobia and aerophobia. They received minimal medications with e.g. Diazepam and Diphenhydramine, both intramuscularly, usually given only once or twice during the disease course following admission to hospital. This was clearly ineffective but there was been a strongly held belief that nothing would be effective.

Clinicians at San Lazaro Hospital have noted that one of the features of furious rabies that is so agonizing for the patient and carers is delirium. In this respect, in addition to the typical hydrophobia and aerophobia, seizure activity and hypersalivation, the features that predominate are *aggression, disorientation, hallucinations, overwhelming terror, hyperexcitability, hypervigilance and confusion*.

The group at San Lazaro is undertaking an observational study to document these symptoms and signs associated with delirium and their progression. Their observations have already resulted in important changes to the way these unfortunate patients are managed.

The San Lazaro observational study has clearly identified that many of the symptoms are psychotic in nature and might therefore better respond to antipsychotic medication (4).

Haloperidol was chosen as being the most easily available and cheapest antipsychotic. This can be given intramuscularly or subcutaneously. See Table 3.

The use of *Diphenhydramine* was continued in an attempt to reduce secretions. In prescribing medications the basic principles for symptom management are applied.

Key Principles

- *Give the most appropriate medication available.*
- *Give REGULARLY.*
- *Give ADEQUATE dosage.*

Difficulties

- *Education of ALL carers in these principles is necessary to achieve consistent and continued symptom control*
- *There are always problems in introducing any change especially in an overburdened, under resourced environment.*
- *Inconsistent availability of even basic medications.*

The prescribing principles, some of the difficulties and the outcomes of improved symptom management are illustrated by the following case examples.

Case example 1

- *A 28-year-old man presented with classical hydrophobia.*
- *He was accompanied by his young wife, pregnant with their 2nd child.*
- *He was terrified that he would die a violent death and his plea was that he would not suffer this.*
- *He desperately wanted to see his 2-year-old daughter before he died.*
- *He was given Haloperidol 5mg intramuscularly IM X4 plus Diphenhydramine 50mg IM X2.*
- *He remained calm and comfortable and was able to see his daughter before he died 36 hours after admission.*

Case example 2

- *A man in his mid 40's was admitted with classical hydrophobia and aerophobia.*
- *He was accompanied by his wife and several extended family members, all very anxious.*
- *He had 4 children aged 21-14 years. His wife could not decide whether they should come and see him.*
- *He pleaded that he should not suffer and expressed fear that his suffering might be a punishment for an affair he had had before he married his wife.*

- *No Haloperidol was available and the patient began to become agitated with early signs of delirium. He was given Diazepam 20mg IM every 2 hours. This settled him. His symptoms began to return and worsen overnight when the medication was not given but improved when reinstated regularly. Symptom control was achieved although not ideal.*
- ***Personal care:** As he was not violent and aggressive bed bathing was possible. This had previously been regarded as too dangerous and patients would die unwashed and in the clothes they arrived in.*
- ***Emotional support:** Discussion between he and his wife was facilitated concerning his affair with forgiveness from his wife and relief for him. His children were also able to see him and say their goodbye.*
- *He died comfortably with his family around him and without the usual barred door locked.*

From the group's experience a simple medication protocol has been developed. See Table 3.

Table 3 MEDICATION PROTOCOL for PATIENTS with RABIES

A: If available:

HALOPERIDOL 5mg IM/SC/IM every hour for 3 doses at least or until patient is calm.
THEN: Continue to give REGULARLY Q6h - Q4h, and 5mg SC/IM prn.
DIPHENHYDRAMINE 50-100 mg IM Q6h – Q4h.

B: IF HALOPERIDOL is NOT available then use
DIAZEPAM 20mg IV/RECTAL M EVERY 2hrs
DIPHENHYDRAMINE 50mg-100 mg IM Q6h – Q4h.

C: Other alternatives to consider:
Levomepromazine 25-100mg SC/IM IM/S.Q4h – Q6hC or
Chlorpromazine 50-100mg IM SC/IM Q4h – Q6h

NOTE:

The key to success is to GIVE MEDICATION REGULARLY, not waiting for distress to recur. The goal is to KEEP the symptoms UNDER CONTROL, NOT to wait until symptoms have returned before giving the next dose of medication. Giving drugs only when symptoms have returned is more distressing for the patient, family AND staff and actually can require more medication in the long run.

The preferable route for Haloperidol is subcutaneous (S.C) as it is less painful and is just as effective as the IM route.

Secretions

- *As previously referred to Diphenhydramine 50 100 mg IM Q6h-Q4h has been used to help control excessive secretions. This was chosen in view of availability and cost.*
- *Other medications that might be considered, are Glycopyrrolate 0.4 mg Q4h SC or Hyoscine butylbromide 10-20mg SC Q6h-Q4h. These anti-cholinergic agents have little central nervous system penetration and thus can reduce secretions without increasing agitation.*

Note: Hyoscine hydrobromide, however, should NOT be used as it may markedly aggravate agitation.

Seizure

- *Seizure activity will require the use of anticonvulsants eg benzodiazepines such Diazepam or, if available, Midazolam.*

Nausea and Vomiting

- *Haloperidol is an effective antiemetic at low doses i.e. 1-3 mg/24hrs. If being used for the symptoms of delirium it will likely then also control any nausea and vomiting. Other antipsychotics also have antiemetic properties at low doses eg Levomepromazine 6.25-12.5mg bd.*
- *If antipsychotics are not being used nausea and vomiting may be controlled with Metoclopramide 10 20 mg SC Q6h-Q4h.*

Fever

- *Fever is usually a more significant issue in the prodromal phase. It can be managed with Paracetamol 1Gm Q6h orally.*

PHYSICAL ENVIRONMENT OF CARE

The room in which the patient is cared for should be as clean, pleasant and quiet as possible, darkened and free from draughts. Chairs should be provided for family members.

When there is confidence that symptom control can be achieved there is less reluctance to attend to these simple measure which can be achieved with minimal cost and which make a big difference to patient and family.

FAMILY COMMUNICATION

As illustrated by the two cases, if symptom control is improved, patient and family can communicate, say goodbyes and deal with "unfinished business". Staff can facilitate this by encouraging open and honest discussion and reassuring families that this is not harmful for the patient and is in fact helpful.

FAMILY SUPPORT

The following are important:

- *Provide a space close to the patients for families to rest, talk and receive support and information.*
- *Honest gentle communication concerning prognosis should be provided.*
- *Emotional support should be given for families who are clearly experiencing a sudden loss, often of the family breadwinners. Any practical advice that can be given concerning social support services that are available close to the family's home is important.*
- *Discussion and provision of important information concerning transmission of disease and indications for post-exposure vaccination. Families need information that the disease is spread by saliva introduced into a wound or mucous membrane and possibly [although not proven] by sexual contact. It is not transmitted through touching intact skin.*

Thus:

  - *Reassure families they can sit with their dying loved one and careful contact will not result in transmission of disease.*
  - *Post-exposure vaccination is recommended for sexual partners and others considered at risk e.g. a contact who has been bitten by or exposed to the saliva of the patient.*

- *When a rabies inpatient's symptoms are well controlled the family may decide to take their loved one home. This may be for purely very important economic reasons. It may be cheaper to transport a live person than a dead body. Families require careful counselling and practical support for this to occur. Support services if available close to their home clearly should be contacted.*

CAREER SUPPORT AND EDUCATION

All health care professionals and other carers involved in caring for rabies patients need education in the following areas:

- *The facts of rabies transmission. In most developing countries pre-exposure prophylaxis is prohibitively expensive. However transmission to health care workers has NOT been reported and is extremely unlikely if normal care is taken and normal precautions for infection control followed. Staff attending to patients' personal care ideally should wear protective clothing with gown, gloves, goggles. However, again if good symptom control is achieved the risk of being bitten or spat at by a patient is minimized.*
- *The principles of palliative care, emphasizing the need for good symptom control with ADEQUATE, REGULAR medication.*

FUTURE

Clearly the best outcome in rabies will be achieved by the continued battle for prevention.

However human rabies will be with us for some time yet. The group at San Lazaro is continuing to collect data on the symptoms, signs and course of rabies patients admitted there and will continue to refine the medication protocol and dosage regimes. We have been surprised that the dose of Haloperidol required to control symptoms has not been much higher.

Education in Palliative Care Principles and the need and possibility for good symptom control in rural areas is important. Clearly many rabies patients die with unrelieved symptoms in rural areas and a simple, affordable, accessible drug regime is vital together with the education to use it. This requires the local organization and political will to resource this. An example of how this can begin is the example of the Department of Health in Manila. The newly formed Palliative Care Group at San Lazaro Hospital are now involved through the Department of Health in providing seminars and education for health care workers from rural areas. Managing rabies patients, by providing good symptom control and family support at home is clearly preferable and should be the ultimate goal of any programme.

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14 Pediatric Issues

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INTRODUCTION

When a child has a life-threatening (LTC) or life-limiting condition (LLC) (i), many are affected. The child, their family, and friends suffer for they are threatened by the possibility of death, and need to adapt to the new situation. Health professionals are impacted by the child's illness and confronted with something they may not be well trained for. It is in this context of multiple vulnerabilities that care should be provided.

The challenge is to transform a potentially tragic experience into an opportunity for growth. If the patient's suffering is relieved, and families' resources explored and put into action, chances are that it will be possible — even in limited-resourced settings.

This chapter attempts to provide a general overview of pediatric palliative care. The first section discusses how morbidity and survival of LTC are affected in developing countries. The following sections review general aspects of symptom control in children and psychosocial isues. Following this, four broad models of care are described. Finally, we describe issues that may arise towards end-of-life (EOL). The Appendixes contain a list of commonly prescribed drugs with their pediatric doses, and symptom assessment scales.

Given the broad range of diseases and symptoms, it is not possible to thoroughly elaborate on each one. The readings and web resources suggested at the end of the chapter are a good starting point for those who wish to expand their knowledge about these issues.

LIFE-THREATENING CONDITIONS IN DEVELOPING COUNTRIES

Main Causes of Death

Although there has been a decline in child mortality rates in the last decades, more than 10 million children, younger than 5 years old, still die each year, most of them from preventable causes. Regional and country variations are wide. Nearly 55% of deaths worldwide occur in just 19 countries and are predominantly linked to pneumonia, diarrhea, and neonatal disorders. In sub-Saharan Africa, malaria is responsible for 20-25% of child deaths, while in South East Africa, AIDS which causes only 0.1% of child mortality globally is the cause of up to 70% of the deaths.

Socio-economic Inequalities

Almost all the deaths of children occur in low-income countries or in poor communities in middle-income countries. It is under these circumstances that about 2 billion children live (87% of the children in the world), and 50% of them are without access to health care and medicines.

Within each country there are enormous inequalities. Socioeconomic differences make children from the poorest sectors bear the greatest burden, while the richest may be comparable to those of industrialized countries. Even inside the poor sectors, the poorest among them have the worst health compared to those that are less poor. No health intervention would be as effective as reducing these gaps.

Prevalence of LTC

In developed countries it is calculated that each year, ten out of 10,000 children, aged 0-19, will have a LTC or LLC, and that one will die. Of those who die, 40% die from cancer, 20% of heart disease, and 40% from other LLC.

Little is known about the prevalence, and regional distribution, of LTC in developing countries. Much of the data come from death certificates, which do not always reflect the underlying disease, and the other data, if collected, is often unreliable. Yet, it is known that children are largely exposed to factors that increase the risk of some LLC such as low birth weight, consanguinity, infections, nutritional deficits, and violence, among others. AIDS, malaria, and some inherited disorders are endemic and highly prevalent in select areas.

By no means are LTC a problem limited to industrialized regions. Developing countries, still struggling with unsolved infectious diseases and malnutrition, are already dealing with their burden and not well prepared for them. The epidemiological transition that many low-income countries are facing, with a rapid increase in chronic and LTC, has placed cancer as the leading non-accidental cause of death in children aged five and over.

LTC's Morbidity and Prognosis

State of the art diagnosis and treatments for LTC are usually expensive, complex and require intensive support care, specialized training, and lab facilities. Therefore, it is more likely that they will be available in large cities, which leaves many children not even diagnosed. Sadly, studies across a wide range of illnesses report that children who receive treatment, achieve initial rates of remission or response comparable to those in the richest settings. Evaluations of long-term morbidity and survival rates in these settings are scarce and hardly comparable to those of developed areas. However, developing countries seem to do worse (Table 1). Possible reasons are high exposure to common infections, poorer nutritional background, and problems with accessibility, though they deserve further study.

Table 1. Reports about survival of selected LTC in different countries*.

Disease	Reports	Source of data
Cancer	Europe, 2002, Gatta et al[1]: 5 year OS of 70-75% in Western and Northern Europe, and of 55% in Eastern Europe.	34 EUROCARE cancer registries in 17 countries and 9 SEER registries in the United States (1985-1999).
	Namibia, 1996, Wessels et al[2]: 5 year OS of 37%	Survey to record all pediatric cancer cases. Namibia (1983 -1988)
	1995, Levi et al[3]: from 1950-19990, childhood cancer mortality rates substantially declined in North America and Australia, but not in Latin American and Asian countries.	Death certification data from the WHO database (1950-1989)
Perinatal HIV-1 infection	Europe, 1997, Blanche et al[4]: 6 year OS of 75%	Primary data from 2 European prospective studies of infants born to HIV-infected women
	US, 1996, Barnhart et al[5]: 5 year OS of 75%.	Medical and social service records (the Pediatric Spectrum of Disease project) of perinatally HIV-infected children (born 1982 –1993)
	Thailand , 2002, Chearskul et al[6]: 5 year OS of 51%	Primary data from a cohort of perinatally HIV-infected children (1994-2000).
	Rwanda, 1999, Spira et al[7]: estimated risk of death at 5 years of 62%	Primary data from a cohort of perinatally HIV-infected children
	Uganda, 1997, Berhane et al[8]: 54% of children died before age 2.	Primary data from a cohort of perinatally HIV-infected children
Cystic Fibroses	Puerto Rico, 1999, Perez-Perdomo et al[9]: MSA of 53.5 months	Secondary data from the Puerto Rico AIDS Surveillance System. Analysis of reported cases (1981-1998).
	US, 2000, Nasr[6]: MSA of 32 years	Review
	Italy, 2002, Assael et al[11]: MSA of 37.7 years	Population-based study in a region with neonatal screening. All CF patients born and followed-up in the region (1938-2000)
	Brazil, 1998, Reis et al[12]: MSA of 12.6 years	Retrospective chart review of all CF patients followed at a hospital (1970-1994)
	South Africa, 1996, Westwood[13]: MSA of 18 years	Retrospective chart review of CF patients followed at a hospital for 20 years
Muscular Dystrophy	England, 2002, Eagle et al[14]: chances of survival to 25 years increased from 0% in the 1960s to 12% in the 1980s, and 53% for those ventilated since 1990.	Retrospective chart review of patients with Duchenne followed at the Newcastle Muscle Centre (1967-2002)
Cerebral Palsy (with severe cognitive disability)	England, 2000, Hutton et al[15]: 63% OS at 35 yrs	Cerebral palsy cohort (births from 1960-1990 in 3 English health districts)
	Pakistan, 1995, Yaqoob et al[16]: 36% died before age 2	Survey (children born between 1984-1987)

* Direct comparisons among studies may not be appropriate. Differences in population, disease identification and staging, or clinical characteristics may account for some of the disparities reported.

References: OS=Overall survival; MSA=median survival age 1. Cancer, 2002. 95(8): 1767-72. 2. Med Pediatr Oncol. 1996 Sep; 27(3): 160-4. 3. Eur J Cancer. 1995;31A(5):771-82. 4. J Acquir Immune Defic Syndr Hum Retrovirol. 1997 Apr 15; 14(5):442-50. 5. Pediatrics. 1996 May; 97(5):710-6. 6. Pediatrics, 2002. 110(2 Pt 1): e25. 7. Pediatrics. 1999 Nov; 104(5):e56. 8. Pediatrics. 1997 Jul;100(1):E7. 9. AIDS Patient Care & Stds, 1999. 13(11): 651-8. 10. Adolesc Med. 2000 Oct; 11(3):589-603. 11. Am J Epid, 2002. 156(5): 397-401. 12. J Trop Pediatr, 1998. 44(6): p. 329-31. 13. J Paediatr Child Health, 1996. 32(4): 323-6. 14. Neuromuscul Disord, 2002. 12(10): 926-9. 15. Arch Dis Child., 2000. 83(6): p. 468-74. 16. Acta Paediatr. 1995 Mar;84(3):267-72.

Palliative Care

Although palliative treatments are indicated when curative (or effective) treatments are not available, it should be kept in mind that the way pediatric end-of-life care is provided has a long-term impact. The experience of caring for a dying child will modify families forever and probably reach into the next generation, as siblings and cousins have their own kids. While trying to reduce inequalities, there is no contradiction in providing appropriate care today.

In these settings, healthcare systems are usually fragmented and disorganized, and respite care facilities and interdisciplinary teams scarce. However, informal community networks may provide the support families need. A religious leader, a teacher, or the major of a small town, could all join "the team". Delivering palliative care may be complex due to the multiplicity of factors involved rather than for the resources needed.

SYMPTOM CONTROL IN CHILDREN

Children can Feel Pain and Other Symptoms

Symptom pathways are present and complete in the fetus around the 20th week of gestation. Therefore, every child is able to feel symptoms from the moment of birth. However, their ability to express them develops over time. Most children will identify and be able to grade symptom intensity by age 5, but this varies according to the child's experience, family style, and culture, among other factors.

Systematic evaluation of symptoms is essential to adequate palliative care (Box 1). Self-report — what the child says she/he feels — is the most valuable assessment tool. Yet, young children, those with impaired communication or denial, are not able to use it. In these cases, behavior should be considered the "self-report" — posture, gestures, vocalizations, and social interaction, the "words"— and the parents their best interpreters.

Crying, moaning, and vocalizing are not the only ways children have to express symptoms. Subtle changes in usual behaviors, communication, or habits such as eating or sleeping may also indicate suffering.

Box 1. Systematic Symptom Assessment

The systematic use of formal and validated instruments to evaluate symptoms should be part of routine clinical care. This standardizes care and makes results comparable. Assessing symptoms and quality of life in children in a systematic way is complex. A "self-report" tool for children should include several versions adapted to the child's developmental level and comprehension, along with their respective parental forms. The latter are necessary not only when children cannot report but also as a complement of children's self-reports. Parents "see things" that children may not see of themselves. Many instruments have been developed to measure quality of life and pain in children, but none has been validated in the palliative care population.

Appendix II includes the only pediatric validated tool that evaluates many symptoms at a time, the "Memorial Symptom Assessment Scale" (MSAS). It was developed for children receiving cancer treatment and has two versions, one for children aged 10-18 and other for kids 7-12. It does not have a parental form and has not been tested in a palliative care setting. However, we present it to encourage its use in children with cancer. The Faces Pain Scale-Revised (FPS-R), a pain intensity scale is also included. FPS-R is easy to reproduce and is valid for 5-18-years old. Compared to other pain scales, FPS-R is more pain-specific (it lacks crying/smiling faces in the extremes), and is easier to score (0-5 or 0-10). It has been translated into 12 languages.

Children are Not Little Adults

Symptom treatment in children has not been systematically assessed, so most of what is currently used comes from the adult literature. Yet, children are not small scale adults, nor are they a uniform group.

Their growth and development involves anatomic, physiological, and psychosocial changes that affect a drugs' pharmacodynamics, pharmacokinetics, and compliance differently from birth to adolescence.

Dosage, drug selection, and side effects pre-emption, must be considered. Doses should be calculated by weight and adjusted by age (Appendix I). Children's vulnerability to side effects should guide drug selection and side effects treatment (Box 2, below).

Non-adherence to treatment is high in children (34-82%) and causes treatment failure. Unavailability of child-appropriate drug presentations (inadequate taste or concentrations), and difficulties with administering meds to kids and teens account for this. Yet, in developing countries, lack of access to medicines prevails. To increase compliance, parents need to understand why, how, and when drugs should be given, and be taught age-adapted techniques. Physicians need to be familiar with those drugs that are not only effective, but also locally available and accessible.

Box 2. Some Examples of Children's Response to Drugs and Their Therapeutic Implications

Compared to adults, opioids produce less constipation, nausea and vomiting, and limiting side effects, and more urinary retention in children. Therefore, kids should receive laxatives if they are going to be on opioids for >10 days, antiemetic treatment should be prescribed if vomiting appears and not preemptively, and urinary retention should be checked for and treated with physical measures, drugs, and/or catheterization, as needed. Need for opioid switch is rather rare but if needed, methadone, hydromorphone, or oxycodone could be used.

Metoclopramide's dystonic reactions are more frequent in children, so domperidone may be a good alternative.

Benzodiazepines' paradoxal reactions are also more common, and switch to phenothiazines is at times necessary.

WHO Recommendations for Cancer Pain Treatment

The WHO basic premises for treating pain in cancer can be extended to the treatment of other symptom's (see Suggested Readings).

Drugs should be administered "by the clock"—on a regular basis— rather than on an "as needed" basis, unless the symptom is sporadic or mechanical. They should be given "by the appropriate route", the simplest, most effective and least painful route; and, they must be titrated "by the child"—when appropriate— until a fair balance between effectiveness and side effects is achieved.

Drug selection should be based on the underlying physiopathologic mechanism and the drug's mechanism of action. In the case of pain, primary analgesics should also be selected "by the ladder", according to the level of pain (ii). Paracetamol, codeine, and morphine are the drugs of choice for mild, moderate, and severe pain respectively.

When available, the oral route should be used. If alternative routes are needed, nasogastric tubes, or rectal administration may be acceptable. They are easy to maintain at home, and relatively inexpensive. The subcutaneous route is a good choice when the enteral route is not an option. This is comfortable for the patient (needles are placed in areas of scarce mobility, and can be changed every 10 days), the procedure is extremely simple, and allows the patient to stay at home.

Non-pharmacological Measures

Symptom perception is the result of multiple interactions among internal and external factors. Thus, symptoms should be targeted with multiple strategies, drugs being only one of them.

Communication is essential to adequate symptom control. Children and families that do not receive an explanation about a symptom's cause and its treatment may feel anxious not knowing what to expect, which in turn, may worsen the symptom.

Kids are particularly susceptible to non-pharmacological methods, e.g. distraction, visualization, relaxation, art, and games. They love being told stories and engage easily in these activities. These tools should be taught to parents for use at home during breakthrough symptoms.

Role of Parents

Apart from interpreting the child's symptoms and monitoring their treatment, parents influence the child's perception and expression of symptoms both verbally and non-verbally. They can sooth —or worsen— their child with simple gestures or words. Thus, empowering parents by making sure they understand the disease and treatments, establishing a supportive environment, connecting them with other parents, and enhancing their social support, will create a better setting for the symptomatic child.

Appropriateness of Treatment

Treating a symptom may involve elevating the symptom threshold —by pharmacological and non-pharmacological methods— or by modifying the underlying cause, e.g. with chemotherapy, antibiotics, transfusions, or a ventilator.

Both types of strategies may be useful to restore quality of life, but when diseases are refractory or advanced, treatments should be carefully considered. Having a given treatment available should not be the reason for prescribing it. Treatments are appropriate as long as they are in agreement with the biologic prognosis of the patient, have an acceptable risk/benefit ratio, and do not prolong agony. Appropriateness varies along the course of a disease, and according to the child's wishes and quality of life.

PSYCHOSOCIAL ISSUES

Caring for a Dying Child

The death of a child goes against the expected. Children are the future, they are supposed to survive adults, continue their labor, and perpetuate the species. Aside from those who are losing a loved one, a child's death may question many of an adult's basic beliefs (justice, religious beliefs), and threaten our expectations of having our dreams and words carried along generations.

For the same reasons, a community may "defend" itself by isolating the family. They may be scared, having no knowledge as to what to do to help. Promoting awareness about medical issues —and what can be done to help these families— usually stimulates collaboration and reduces discriminatory attitudes.

Each Child is Unique

Each family will explain and integrate death in a singular manner, according to their history, cultural background, and socioeconomic context. As health professionals, we should be able to leave out our own values and judgments, and provide those that are significant for the families.

Children are Children Until They Die

They have a right to play, do their favorite activities, and be in contact with their loved ones. They also have the right to be protected from bad news —if they wish so. Parents or caregivers are the ones legally authorized to make decisions on their behalf and can act as a filter of the outside world in these situations.

On the other side, if children want to participate in their medical care they should be allowed to do so. Information should be tailored to their age, level of development, and ability to understand. Parents should be present and allowed to lead the discussion with the child if they wish. Delivering information through playing, computer games, or story telling is especially useful, as it allows children to process the information better.

Parents Will Have a Difficult Time Accepting That Cure is No Longer Possible

Merely insisting that cure is no longer possible may create barriers and hinder parents shift of goals. Rather, listening to their hopes and allowing them not to give them up, helping them seek second opinions, and pointing out the child's —and their own— suffering may allow parents to slowly change their hope of a cure to one that is more realistic, e.g. hope of diminishing suffering, or accomplishing something meaningful. In order for health care professionals to support parents in this way, they need to accept themselves that cure is not possible and offer palliative strategies. If during the whole course of the disease, curative and palliative goals have been targeted concurrently, everybody will be more likely to accept the situation without considering it a "failure".

Some parents will not accept their child's impending death at all. In such cases, letting them maintain hope for a miracle, while focusing on the child's comfort, may be the best we can do for that family.

When cure is no longer possible, uncertainty appears forcefully. How and when, will the disease progress, when will death occur, or how is the family is going to feel afterwards, are frequent unanswerable questions. Listening to parent's worries and focusing on living day by day may alleviate their sorrow. Some degree of appropriate denial is necessary and permits parents to keep up with daily activities while at the same time feeling happy with whatever achievements the child and family attain.

Some families may have severe social or psychopathologic disturbances and/or very high and persistent levels of denial. In such cases, creating alternative ways of support with relatives, neighbours, and community resources may be the only way of providing for the child's best interests.

Siblings

Parents, who are concerned and overwhelmed with the care of the ill child, may often pay less attention to their healthy children. Siblings are therefore doubly affected. They suffer because of their brother's illness —although this is not always noticeable— and also for feeling "deserted" by their parents. Parents should include them in discussions about the disease and also try to give them some quality time. Sometimes siblings need to maintain their routine and prefer not to be greatly involved in these discussions. In these cases, parents should respect their style while providing them with information in an age-appropriate manner.

Communication is Crucial to Establish a Good Family-team Rapport.

Parents are carers but also need to be cared for

Parents need to be well informed because they have to take part in the decision-making process, but at the same time, are deeply affected by their child's disease. This double role needs to be acknowledged and information should be delivered in an honest, respectful, and caring manner, checking frequently for understanding. Length of interviews and quantity of information should be adapted to a parents' needs. Some want, and seek, detailed and updated information while others only want step-by-step facts. Parents' style should be respected and their reactions —anger or sorrow, being puzzled or in shock— allowed since this is the way they have to cope with the situation.

If available, contact with parent's associations or other organizations should be facilitated, and booklets and other sources of information provided, as all may help them feel supported and less isolated.

Children understand what is going on

Children are very sensitive to what their caregivers feel and express. Seriously ill and dying children are much more aware of their illness and prognosis than it's usually acknowledged. They always know that something unusual or bad is happening. Depending on their age and developmental level they will express their feelings differently, but if we pay close attention to verbal and non-verbal cues and give them the opportunity to communicate, we may discover they have things to tell us.

Planning a Palliative Care Strategy

When cure is no longer the goal of treatment, many things change. Restrictions, routines, and efforts imposed by treatments become meaningless. Care can take place at a variety of places —home, hospital, and hospice. Parents and children generally prefer home, though this may vary according to the child's condition and the broader context. In developing countries with centralized health systems, home may be hours away from the hospital. Fears of being far from familiar doctors and nurses may interfere with the family's wishes of going back. Health professionals can support families by helping them explore their fears regarding going back home —since many may be worked out— and by assuring continuity of

care. In order to do so, itmay be helpful to build a "bridge" between the different settings by including, or contacting, clinicians and nurses who will be involved in EOL care at an early stage of treatment.

Palliative care strategies should be family-centered, designed to fit the family's changing needs, and appropriate to their context. They should be flexible, include the whole process of care, and be thoroughly discussed with parents (Box 3).

Box 3. Planning a palliative care strategy for children with advanced LTC	
Before planning, be familiar with:	
1.	Family resources, history, previous ways of dealing with losses, coping style, existing or potential social support.
2.	Kid's disease course and response to treatments, role in the family, access to and ways of coping with information and the disease itself, child activities (school, play, sports, relation with peers).
3.	Regional health care and community resources
Plan should be family-centered —tailored to the family's characteristics and resources— and include:	
1.	A plan to deliver information: delivery of news is a process and may take several encounters. Plan ahead why, how and what to share, and who will be present
2.	Involvement of families in the decision making process: they should actively participate in decisions about how and where care will take place
3.	Symptom control: pay attention to every symptom at every stage of illness evolution, treat them actively and monitor treatment
4.	Emotional support: child and parents have the right to receive counseling and emotional support in case they want, or the team evaluates they need it.
5.	Focus on healthy areas: school, artcrafts, films, writing, etc. There are many things very ill children can do and enjoy.
6.	Help with practical and financial problems: everyday activities (e.g. grocery shopping, laundry, taking care of the siblings, money for transportation) may bring up a lot of stress if help is not available.
7.	Anticipation of problems: information about forthcoming events helps families to be prepared.
8.	Respite care strategies: when long-term care is expected, respite should be strongly encouraged.
9.	Bereavement follow-up: the more parents are able to stay with and support the child, the better prepared they will be to face the bereavement process. Strategies may vary depending on resources available. At least, families should be contacted after death to give closure and check for signs of pathological grief.

Planning a Palliative Care Strategy When Life-expectancy Is Long

Many LTC evolve over years, making necessary some degree of family reorganization to cover the child's needs. Families may decide that they prefer to move their residence in order to have greater access to care. One parent may need to become a full time carer and the other to take charge of the family's financial support. Each of these movements involves losses (of support, belongings, or personal expectations) and adjusting to them will require effort and time.

Caring for a child for long periods is overwhelming. As carers become exhausted, both the child and carer's vulnerability increases, leading to a circle of greater health needs and more exhaustion. Despite being worn out, some parents feel so guilty about leaving their child —even for short times— that they cannot even think about taking some rest or enjoying leisure activities.

Respite (carer's rest) should be strongly encouraged when long-term care is expected. It is essential to maintain the families' physical and emotional health which can be especially important for siblings. There are many ways of providing respite care that may function well. Which one is used will depend on the child's needs and system possibilities. Extended family, friends, voluntaries, or nurses may care for the child during certain hours, or night shifts. There may be institutions available for day care or longer stays. Flexibility in family members' roles, and the possibility of developing formal and informal sources of support (school, family, friends, community), may predispose to greater chances of adapting successfully to the child's illness.

Frequent Misconceptions About Palliative Care

There is a "good" way to go through this experience.

Almost everybody working in the field has an "idea" about what is a "good death." However, it is important to keep in mind that families go through it as they can. Our role should be to assist families in using their own resources.

Incurable equals dead.

When told that the child is not going to be cured, parents may interpret that death is imminent, which is usually not the case. This should be clarified. Expecting death on a permanent basis may prevent the family from focusing on healthy areas or carrying out activities —trips, "get togethers", or celebrations— that can add meaning and comfort to the child's life.

Psychosocial aspects are mental health specialist responsibility.

Emotional aspects are a team's responsibility. Everyone must be aware of the psychosocial aspects of care and consider them in every intervention. Nevertheless, a specialist is required if:

- *A family member has a suspected, or diagnosed, psychopathologic disturbance before diagnosis or during treatment.*
- *Families develop severe dysfunctions, show poor compliance, or difficult relationship with the team during treatment.*
- *The child has uncontrolled symptoms*

It is better to die at home than at hospital.

It is usually believed that an ideal death should take place at home surrounded by our loved ones. Yet, this is not always what families consider ideal when real death approaches. A child may have uncontrolled symptoms, or parents may be scared of having to deal with emergencies, may not want siblings to be involved, or may not have the support they need to stay at home. Although each of these may be potentially solved, at times, the hospital may be the only environment that parents, or the child, find calm and supportive. If this is the case, the family's wishes should be respected. Home is a good place to live. Where each one dies is less important than how, and with whom they do it.

MODELS OF CARE

The type of care a child and the family needs —intensive, curative, palliative or a combination of all— at any time throughout a disease, depends on the diagnosis, disease course, family wishes, and available treatments. Based on some common characteristics, the Bristish Association for Children with Life-Threatening Conditions (ACT) and the Royal College of Pediatricians described four different models of care. We will present a general description of each group followed by pertaining features of palliative care delivery. Groups are broad and include different diseases. Some examples are given for each category. In developing countries, diseases may fall in different categories depending on which treatments are available.

Model I : Illnesses for which a Potentially Curative Treatment Exists

Cancer, organ failures (renal, hepatic, cardiac), and malaria are the leading examples in this category. Conditions in this group share a possibility of cure, but their course and manifestations vary widely. Although cure-oriented treatment is predominant at diagnosis (Figure 1), palliative strategies should also be included early to improve quality of life. If disease progresses, palliative measures gradually take over.

Disease-related symptoms are prevalent at diagnosis

The onset of a disease is usually associated with distressing symptoms (pain, vomiting, fever, asthenia, etc). Many symptoms disappear shortly after disease-directed therapy is started. Yet, it may take days or weeks for this to happen, so symptom-oriented treatment should be instituted concurrently and monitored frequently. On occasions, symptomatic treatment is needed for a long time.

The way in which diagnosis is transmitted to families impacts on their compliance with treatment

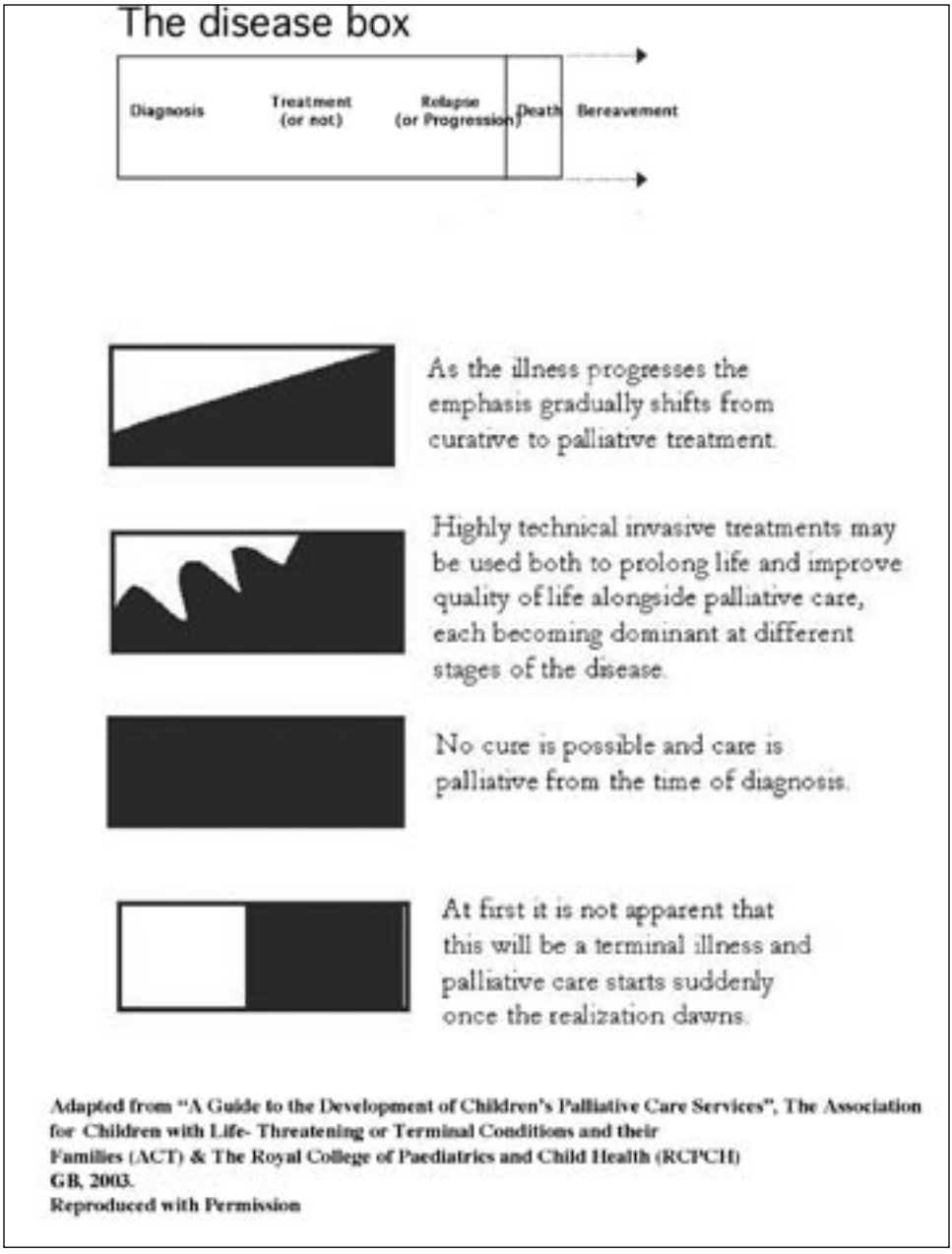
Communication with the child and family at this time is critical. Having a previously healthy child diagnosed with a LTC is a major twist for any family. It will take them time to understand and accept the new situation. The effects of diagnosis disclosure are long lasting. The parent and child's ability to cope with a diagnosis and adherence to treatment is largely affected by these first encounters.

During treatment, symptoms should not be overlooked

While cure-oriented treatment is being delivered, palliative strategies are often neglected. Families gradually become more familiar with the disease, its treatment, and the healthcare system, having thus, a new "normal life" which includes the LTC. However, children may have many symptoms, predominantly related to treatments. Psychological symptoms are also frequent, and may be a way of realizing the impact that disease and treatment made on their lives. Many cause high levels of distress and should be addressed aggressively as they affect the quality of life at a time when the child is potentially able to enjoy a lot of activities.

When group I diseases become refractory, goals should shift towards palliation.

As the disease progresses, symptoms become prevalent and usually cause a lot of suffering – e.g. during the last month of life, 50% of children with cancer have ≥3 symptoms that cause high levels of distress. Therefore, they should be treated promptly. Invasive procedures and treatments – e.g.


The disease box
Diagnosis
Treatment (or not)
Relapse (or Progression)
Death
Bereavement
As the illness progresses the emphasis gradually shifts from curative to palliative treatment.
Highly technical invasive treatments may be used both to prolong life and improve quality of life alongside palliative care, each becoming dominant at different stages of the disease.
No cure is possible and care is palliative from the time of diagnosis.
At first it is not apparent that this will be a terminal illness and palliative care starts suddenly once the realization dawns.

Adapted from "A Guide to the Development of Children's Palliative Care Services", The Association for Children with Life- Threatening or Terminal Conditions and their Families (ACT) & The Royal College of Paediatrics and Child Health (RCPCH) GB, 2003.
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chemo or radiotherapy, or surgery – may be of value if they can reinstate a function, or relieve a symptom, in a logical amount of time, and if suffering is outweighed by the benefits obtained.

The course of disease progression varies greatly among diseases and individuals. It may take weeks, months, sometimes years. Frank deterioration, or compromise of vital organs, may alert that the

EOL is approaching. At this point, less aggressive treatments, as blood works, blood transfusions, or antibiotics, may also become futile. If they are not able to improve quality of life for a reasonable period, procedures should be stopped and more suitable diagnostic (e.g. clinical signs) or therapeutic measures (e.g. sedation) used.

Model II: Includes chronic, progressive conditions for which there are intensive treatments that may prolong life and allow participation in normal childhood activities, but premature death is still possible

Chronic respiratory diseases, neuromuscular disorders, and AIDS are some examples. Recent developments in antimicrobials and ventilation therapies have dramatically changed their course and significantly increasing life expectancy. Patients who used to die as teenagers, may now be able to reach their 3rd or 4th decade of life. In developing countries, apart from treatment availability —which is not homogenous— common childhood illnesses frequently cause premature deaths in these children.

Primary goals of treatment are to extend life and improve its quality

Most of these conditions are diagnosed during the first years of life. Severe forms, or those occurring in limited-resourced settings, may render to rapidly progressive courses. More frequently, patients need increasing levels of treatment to maintain health, until a limit is reached, and death becomes more likely. Intensive restorative treatments alternate with palliative strategies over years depending on which is more appropriate according to the patient's status (Figure 1). The goals of treatment are to maximize quantity and quality of life, and delay the onset of the terminal phase. To do so, vital organs functions should be maintained as intact as possible. Physical therapy is critical to improve respiratory function, muscular strength, speech, and swallowing. Other examples of appropriate intensive measures are mechanical and positive pressure ventilation, antimicrobials, antiretrovirals, tracheotomy, surgical correction of scoliosis, and pacemakers. Defining when these treatments are no longer appropriate is not easy at all, because of the slowly progressive nature of these illnesses. Decisions should be made by a team and tailored to the child's situation and wishes.

Learning to live with a chronic disease includes adaptations at many levels

Families faced with group II diseases not only have to accept incurability at the time of diagnosis, but also learn that multiple family members are, or may, be affected. They need to deal with social issues, e.g. in HIV, or rethink family planning in neuromuscular diseases. Handling all these aspects is difficult. Denial, favoured by a frequent paucity of symptoms at this stage, or guilt due to their inherited or contagious nature, is frequently present and may further hinder coping.

During the course of the disease, the parents, the child as well as the siblings, have to shift their expectations and ideals into more realistic ones and accept the child with his/her current limitations. Each sign of progression of the disease requires a new adjustment. Although emotional support by a specialist is not always needed, in moments of crisis or change it may help families to cope with these multiple losses.

Dyspnea and pain are the main symptoms in group II illnesses

Between 50-85% of children with respiratory conditions, AIDS, or neuromuscular disorders suffer pain and dyspnea. Symptoms are more common near EOL.

Opioids should be introduced rather early. Otherwise, when treating dyspnea in an exhausted but opioid naïve patient, the chance of inducing respiratory depression would be unreasonably high. Relaxation techniques should also be part of early care plans. They are useful for asphictic crises and results are better if patients are familiar with them (Box 4).

Box 4. Non-pharmacological measures for asphictic crisis

- Stay calm and close to the child, hold his/her hand if she/he wants to, or put a hand softly over his/her shoulder to transmit support and security.
- Do not leave the child alone and assure somebody is going to watch his/her sleep.
- Maintain the child in a 45° position using pillows if necessary.
- Dress the child with loose clothes.
- "Give air":
  - o Keep at a minimum the number of people in the room.
  - o Use a fan (or paper-fan) to give air in the face, open the windows.
  - o Facilitate breathing control: When suffering an asphictic crisis the child looses control. Help him/her to get it back. Begin by firmly but calmly saying: "Put air in with your nose and leave your breath out by the mouth". Use colloquial words. The pace at which the sentence is said, should match the child's breathing. Once your words are coordinated with the child's breathing, they should gradually slow down. Begin to order longer exhalations by stretching the words: e.g. "leeeave your breath oooout". If sentences are firm and clear, the child will be able to catch up the verbal rhythm and reduce tachypnea.

Model III : Chronic, progressive conditions for which there are no curative or intensive treatments available

This group comprises more than 50 progressive diseases that usually extend over years and tend to affect the central nervous system. Lysosomal and peroxismal disorders (neurodegenerative and storage diseases) fit this model of care. Although similar to group II, these LLC used to have no intensive treatment options and therefore primary treatment goals were exclusively palliative (Fig.1). Yet, the latest developments in organ transplant, enzyme replacement therapy, and gene transfer are changing dramatically their life expectancy and clinical course. Although very promising, these therapies still haven't proven their full short and long-term effects, and their high costs preclude their use in low-income countries.

Children are progressively affected in multiple domains of function depending on the nature and extent of their underlying disease

These entities may be diagnosed at birth or appear after a period of normal development. Their life course and clinical manifestations vary greatly. As a rule, the earlier they manifest, the more severe and rapidly progressive they are. The goals of treatment are to improve the child and family's quality of life by controlling symptoms, reducing the child's vulnerability, and enhancing the child's autonomy. Physical therapy, speech therapy, and pharmacological treatments are all appropriate measures. If not treated, children habitually die in early childhood or as teenagers due to acute infections, encephalopathy, or because of respiratory, cardiac, or liver insufficiency. Spasticity, seizures, pain,

constipation, and dyspnea are common throughout these illnesses.

Maintaining adequate nutrition and sleep are paramount to improve these children's quality of life

Feeding problems associated with impaired oral-motor dysfunction are almost universal, and worse in patients with severe neurological affection. They frequently lead to malnutrition which increases the child's morbidity and symptoms. Sleep disturbances are also highly prevalent and are triggered by behavioral problems, upper-airway obstruction, epilepsy, or nocturnal feeding or medication. Lack of adequate sleep affects not only the child, but also his carers.

Because of their cascade effects on the child and carers, these problems should be addressed early and aggressively. Both maintaining an adequate nutritional status — using physical therapy, thickening food, giving supplements, or placing a gastrostomy— as well as restoring a normal sleep pattern —by imposing bedtime routines, reduced or relaxing stimulus, or giving hypnotics— is critical.

Caring for a child with a LLC involves huge emotional work

As in group II, these families also have many difficult issues at diagnosis, such as accepting the irreversibility of the illness, dealing with inheritable conditions, giving up the ideal child they have been dreaming of, or the healthy child they had, and planning how to deal with long-term care.

Many of these children depend on their parents for almost everything, from communication to basic needs and entertainment. This multiplicity of roles (carer, interpreter, parent) may increase the parents' vulnerability. Signs of burnout and pathological grief should be regularly checked for.

Model IV : Includes children with severe, irreversible, and non-progressive cognitive and/or motor disability, whose increased vulnerability may lead to health complications and premature death

Cerebral palsy or disability due to spinal cord injury, are usually a result of accidental/preventable, or treatable events such as trauma, violence, hypoxia, malaria or tuberculosis. Palliative strategies can help to improve the quality and the quantity of life and should be a strong focus of treatment (Figure 1). Sometimes intensive measures may be of value, depending on the quality of life and desires of the family and child. As in model III, long-term care issues should be discussed with these families as well.

Clinical course of these conditions is mainly stable, but symptoms may limit the patient's ability either physically or socially

Feeding problems and sleep disturbances are also highly prevalent in this group and their treatment is crucial to lengthening survival. Spasticity and drooling are present in more than half of the kids and are major social problems. They should therefore be addressed assertively with physical therapy, positioning techniques, and pharmacological treatments.

Neurological signs and symptoms may not only limit a patient's capacities, as happens with mental retardation or motor disabilities, but also lead to social isolation. Children with sensorial loss,

epilepsy, and behavioral problems are frequently discriminated against. Physical therapy and early inclusion in school activities and rehabilitation programs will help them develop to their maximum capacity. If this is not possible, treatment still may be useful to ease the task of caregivers.

Parents, and many times the child, will need to accept a "different child"

As these conditions appear suddenly in previously healthy children —unless it is a perinatal condition— parents have to grieve for the loss of the child they had, along with accepting that she/he is the same although with different conditions and capacities. Another important task is to abandon the expectations of a reversion of the process. Both may be difficult and long processes for some families.

Treatment decision has to consider long-term effects and patients' wishes

As these conditions are non-progressive, long-term consequences of symptoms and treatments need to be considered when evaluating an intervention.

There is not a terminal phase as such, as it is not the disease that will cause death. Death may be premature (caused by an acute event), or a result of the combination of spasticity, scoliosis, repeated infections, and malnutrition, among others. Final events are usually acute infections — emergencies— where there is no time to "think". Therefore, it is crucial to discuss in advance what type of treatment would be instituted should an acute event present (antibiotics, oxygen, ventilator).

Since families and the child may change their minds over time, these discussions should be updated regularly.

APPROACHING END-OF-LIFE

The terminal phase, when death is imminent, may last from hours to a few days, sometimes a week. During the EOL period, the goal is to achieve maximum relief in the shortest possible time.

Emergencies

Emergencies may be the final events of a child's life. During an emergency, the distress is too high to think effectively. Anticipating them, will allow families to deal better with the crisis. Discuss in advance possible emergencies or symptoms that may come up at home (asphictic crises, bleeding, and seizures); pharmacological and non-pharmacological measures for use in the home (rectal anticonvulsants, relaxation and breathing techniques, possibility of using sedative drugs); provider(s) to be contacted; center that will receive the child; means of transportation; arrangements needed to be taken of care for house chores and other children.

Withdrawal

Parents need to know that as death comes close, children tend to withdraw and interact scarcely with the outside world, and eat and drink less —if at all. Parents are greatly distressed by these, as communication and feeding are essential to parenting. They should be advised that withdrawal is normal and not a sign of anger or conflict, that feeding is given for pleasure and to prevent hunger, and that hydration may be needed when thirst or signs of reduced drug clearance e.g. sedation, exist.

Children Need Permission to Die

Children do not like to disappoint their parents. They may feel guilty of not being able to "defeat the disease", a battle parents —and doctors— may ask them to fight. When parents can let go and say goodbye, reassuring the child that it is OK to rest and die, the children die more peacefully.

Children do not Need to be Asleep to Die

Kids may be able to take oral meds and be awake until shortly before death. This should be encouraged, at home or in hospital, as it is more natural and comfortable.

Only if symptoms are intolerable, acute, or if life-threatening events take place (e.g. asphictic crisis, massive bleeding, fitting), are sedative drugs necessary (Box 5).

Box 5. Some considerations about sedation

Death may occur shortly after administering sedatives, raising guilt in parents and us. However, children do not normally die after receiving an appropriate dose of sedatives. If they do so, it is probably due to their extreme fragility, which makes any minimal stimulus —drugs or symptoms— enough to cause it. As it is not possible to know in advance when death will occur, it is right to try to relieve a distressed child.

Before proceeding to sedation, families should be thoroughly informed and involved in the decision. Both the objectives of sedation and the chance of death must be addressed. These discussions may be difficult, as they involve letting go. Having had previous discussions is crucial. Helping parents recall their wishes —e.g. not to prolong suffering— may let them feel more comfortable with the decision. If the child is awake, she/he should be explained that they will be given a medication that induces sleep. Some children go further with discussions and want to know whether they may die. They deserve honest and caring answers.

CHILD CARE IN DEVELOPING COUNTRIES

Caring for dying children in developing countries is difficult. Patients are not only dying but they also suffer from poverty, hunger, having little education and safety. Health professionals are usually overworked, underpaid, and many times have very limited resources.

This combination may result in high levels of frustration and burn out. Incorporating palliative care strategies into routine clinical care, not working alone, and developing international networks are ways of transforming a difficult job into a more rewarding one. Health workers, often trained to "do something", may find it easier to accept the irreversibility of a condition if they have something to offer. Sharing decisions with others —colleagues, family, traditional healers, community— not only lessens the burden but also brings new perspectives which may be better for the family. International collaborative networks including centers from both developed and developing countries may result in valuable ways of sharing experiences and developing research, an imperious need in the field. Finally, living one's life as fully as possible is also a great source of satisfaction and helps one cope better with this challenging job.

CONCLUSION

Little is known about LTC in developing countries. Attention should be given to pediatric palliative care in both industrialized and developing countries where treatments are scarce, usually confined

to large cities, and the poorest have less access to them, making morbidity and prognosis apparently worse.

Pediatric palliative care should be provided to any child with a LTC or LLC from the moment of diagnosis —regardless of the outcome of the disease— with the appropriate balance between curative or intensive approaches. The goal is to achieve the best possible quality of life for the child and support their families throughout the course of the disease. Strategies should be family-centered and include control of distressing symptoms, provision of respite, and care through death and bereavement. Four different models of care have been described based on the child's underlying condition, chance of cure, and estimated length of survival.

Footnotes

(i) Life-threatening conditions: illnesses that can be cured but may lead to death. Life-limiting conditions: those for which there is no cure and will cause death sooner or later.

(ii) Comment: it is not necessary to ascend the ladder step-by-step. Rather, it seems more appropriate to think of an "analgesic elevator" that leads directly into the appropriate drug for that level of pain.

Suggested Readings

1. Cancer pain and relief and palliative care in children. Geneva, World Health Organization.(1998).
2. Textbook of Pediatric Palliative Care. Eds. Hain R, Goldman A, Liben S. (in press).
3. Jankovic, M., T. Eden, et al. (1999). "Guidelines for assistance to terminally ill children with cancer: a report of the SIOP Working Committee on psychosocial issues in pediatric oncology.[comment]." Medical & Pediatric Oncology 33(4): 395-8.
4. Spinetta, J. J., M. Jankovic, et al. (1999). "Guidelines for a therapeutic alliance between families and staff: a report of the SIOP Working Committee on Psychosocial Issues in Pediatric Oncology." Medical & Pediatric Oncology 32(1): 44-8.
5. Spinetta JJ, Jankovic M, Ben Arush MW, Eden T, Epelman C, Greenberg ML, Gentils Martins A, Mulhern RK, Oppenheim D, Masera G. "Guidelines for the recognition, prevention, and remediation of burnout in health care professionals participating in the care of children with cancer: report of the SIOP Working Committee on Psychosocial Issues in Pediatric Oncology." Med Pediatr Oncol. 2000 Aug;35(2):122-5.

Web resources:

1. ACT: http://www.act.org.uk/pages/start.asp .The site of the British Association for Children with Life-Threatening Conditions (ACT) has plenty of material about pediatric palliative care. Some of the resources include Guidelines to develop pallative care services, a discussion list, and Symptom Control Guidelines.
2. The Pediatric Pain Sourcebook: http://painsourcebook.ca/
3. Fundación Natalí Dafne Flexer: www.fundacionflexer.org (material in Spanish)

Appendix I

Pediatric palliative care frequently used drugs

Doses in this section have been checked with current literature (Aug 2003). However, as doses, indications, and side effects may change over time, it is the prescriber's responsibility to check the data befor administering the drugs.

DRUG			Dose (mg/kg/dose)[1]	≥12 years old or 40 kg (mg/dose)[1]	Max daily dose	Interval	Route[2]
Analgesics							
NSAIDs		Paracetamol	10	500-1000	4 g	4-6hrly	po/r
		Aspirin	10	500	3,6 g	4-6hrly	po /iv
		Naproxen	5	250-500	1 g	12-hrly	po
		Ibuprofen	10	400	1.8g	6-8hrly	po/iv/im
		Diclofenac	1	50-75	150mg	8-12hrly	po/iv
OPIOIDS	Weak	Codeine	0.5-1.5	30	240mg	4-6hrly	po
		Dihydrocodeine	0.3-1	30	180mg	4-6hrly	po
	Strong	Morphine Immediate release	<1yr: 0.08 1-12yr:0.2-0.4	10-15	No maximum dose[5]	4hrly	po/r
			0.05				iv slow/sc
		Controlled release[3]				8-12hrly	po
		Oxycodone[4]	0.2	5	400mg	4-6hrly	po
		Methadone	0.2mg/kg	5-10		12hrly	po
		Fentanil	1-2µg/kg	5-10µg/kg		Continuous	iv
ADJUVANTS[6]		Amitriptyline[7]	0.2-1	25	150 mg	Nocte	po
		Carbamazepine	5-10	100	1200 mg	8-12hrly	po
		Sodium Valproate	5-10	200	35 mg/kg/day or 2g	8-12hrly	po
		Clonazepam[8]	0.01-0.05	0.5	4 mg	12hrly	po
ANTAGONISTS							
Opioids:		Naloxone	0.01-0.02[9]	0.4		2'–3'	iv
Benzodiazepines:		Flumazenil	0,1- 0,2	1		15'' y 30''	iv

References:

[1] Choose whichever is the smaller dose from these two columns

[2] Routes: po=oral; iv=intravenous; im=intramuscular; sc=subcutaneous; r=rectal; sl=sublingual

[3] Dose calculation= Daily total morphine dose (mg)/2-3 (depending if dosing 8 or 12 hourly)

[4]Doses for opioid naïve patients. In patients receiving opioids, divide by 12 the daily total morphine dose. Once effective doses are reached, convert to modified release preparations if available.

[5]Doses suggested for opioids are initial doses. They must be titrated against pain and side effects. When pain is not relieved, increase dose by 30-50% if using short acting opioids, until an effective dose is reached. If using long-acting opioids, use extra doses of short acting drugs (equivalent 10% of total daily dose), and adjust long-acting opioid dose the day after (calculate equivalent morphine total daily dose given and convert).

[6]Adjuvants doses must be titrated against pain and side effects. Evaluate every 48-72 hrs.

[7] Before starting amitriptyline conduct EKG to rule out conduction defect.

[8]Clonazepam (useful for neuropathic pain) its better administered at noon and nocte because of its sedative effects.

[9]In patients chronically receiving opioids, begin with 0.002 mg/kg and repeat until respiratory rhythm is recovered.

Appendix I, cont.

DRUG	Dose (mg/kg/dose)[1]	≥12 years old or 40 kg (mg/dose)[1]	Max daily dose	Interval	Route[2]
Antiemetics					
Metoclopramid	0.1-0.25	5	0.5mg/kg	8hrly	po /iv
Domperidone	0.2-0.4	10-20	1.6 mg/kg	4-6-8hrly	po /iv
Levomepromazine (Methotrmeprazine)	0.125	2.5-25	1mg/kg	12hrly	po/ sc/iv
Haloperidol	0.025-0.05	1.5	0.1mg/kg	12hrly/nocte	po
	0.025-0.05 mg/kg/day			continuous	sc/iv
Ondansetron	<0.3m^2: 1mg/dose	8		8-12hrly	po
	0.3-0.6m^2: 2mg/dose				
	0.3-0.6m^2: 2mg/dose				
	>1.2 m^2: 8mg/dose				
Cyclizine	>5 years: 25 mg/dose	50	150mg	8hrly	po
	1mg/kg/day	50	100mg	continuous	sc
Hyoscine Hydrobromide[8]	0.3	0.3		6hrly	po/sc/ iv/sl
Hyoscine Butylbromide	0.6	10		4-6-8-12hrly	
Drugs used for drooling					
Glycopirrolate[9]	0.04		0.4 mg/kg	8-12hrly	po
Trihexyphenidil[10]	0.02-0.04		0.3 mg/kg	8-12hrly	po
Drugs used for opioid induced vesical retention					
Bethanecol	0.2-0.5	10-25	0.4 mg/kg	8-12hrly	po
Muscle relaxants					
Diazepam[11]	0.1-1mg/kg/day	5mg	40mg	6-8-12hrly	po/iv
Baclofen[12]	0.2 mg/kg or 2.5mg/dose	5 mg	30	6-8hrly	po
Steroids					
Dexamethasone[13]	0.2		0.5mg/kg Max: 18	Morning[14]	po

[8]Useful if a cinetosic component is present. Also used to reduce bronchial secretions.

[9]Increase dose every 10-14 days. Also used to reduce bronchial secretions.
[10]Indicated in patients with drooling + rigidity. Increase dose every 10-14 days.

11Increase benzodiazepines every 48-72 hs until an effective or the maximum daily dose is reached
12Increase baclofen (use in >12 years old) 2.5-5 mg every 48 hs until an effective or maximum dose is achieved.

[13]Steroids should be used only in short courses (3-5 days) and then suspended. Useful for pain due to nerve compression and hepatomegaly, and increased cranial pressure related symptoms.
[14]If dose is too large, give at a.m. and noon. Avoid later doses to reduce irritability and sleep disturbances

Appendix I, cont.

Laxatives[15]					
Lactulose (softener)	<1 yr: 2.5ml 1-5 yr: 5ml 5-12yr: 10ml	15ml	30ml	nocte	po
Docusate (softener)	1.5 mg/kg	100 mg	5 mg/kg or 300mg	nocte	po
Bisacodyl (stimulant)	2.5mg/dose	5mg	10mg	nocte	po/r
Sodium picosulphate (stimulant)	<4yrs: 0.25 4-10 yrs: 2.5-5mg/dose	5-10mg	10mg	nocte	po

[15] An association of a stool softener with a stimulant laxative is usually needed.

SEDATION PROCEDURE IN CHILDREN

Opioids and benzodiazepines used for sedation should be short acting and with rapid onset of action. Therfore, an association of morphine and midazolam is suggested, but may be substituted by other similar drugs. Midazolam should be administered first, followed 5 minutes later by morphine. Unless an intravenous access is available, drugs should be given subcutaneously. Initial doses are:

1. ***Midazolam****: 0,05 mg/kg (iv or sc)*
2. ***Morphine****: 0,05 mg/kg. (iv or sc), or ½ the oral morphine dose (if receiving other opioid, calculate the equivalent parenteral morphine dose). If child is morphine naïve, start with a lower dose (0.01 mg/kg).*

This regimen can be repeated every 5 minutes until sedation is obtained. If a continuous infusion is required then recommended initial doses are:

1. ***Midazolam****: 0.05 mg/ kg/ h (iv or sc)*
2. ***Morphine****: calculate the equivalent daily parenteral dose of morphine based on the patients' current opioid intake (e.g. if patient is on oral morphine divide oral daily dose by 2) and then by 24 to obtain mg/h of parenteral morphine. In morphine naïve, start with 0.01 mg/kg/h.*

Initial doses must be titrated about 30% every ten minutes until relief or sedation is obtained.

APPENDIX II.
Memorial Symptom Assessment Scale (MSAS)

MSAS (PEDIATRICS 7–12)
NAME_____MRN_____ DATE_____
Instructions:
We want to find out how you have been feeling the last 2 days Use a pencil or crayon to circle your answers

1. Did you feel more tired yesterday or today than you usually do?
YES or NO
If YES:

How long did it last?	1-A very short time	2-A medium amount	3-Almost all the time
How tired did you feel?	1-A little	2- A medium amount	3- Very tired
How much did being tired bother you or trouble you?	0-Not at all	1-A little	2- A medium amount	3- Very much

2. Did you feel sad yesterday or today?
YES or NO
If YES:

How long did you feel sad?	1-A very short time	2-A medium amount	3-Almost all the time
How sad did you feel?	1-A little	2- A medium amount	3- Very tired
How much did feeling sad bother you or trouble you?	0-Not at all	1-A little	2- A medium amount	3- Very much

3. Were you itchy yesterday or today?
YES or NO
If YES:

How much of the time were you itchy?	1-A very short time	2-A medium amount	3-Almost all the time
How itchy were you?	1-A little	2- A medium amount	3- Very tired
How much did being itchy bother you or trouble you?	0-Not at all	1-A little	2- A medium amount	3- Very much

4. Did you have any pain yesterday or today?
YES or NO
If YES:

How much of the time did you have pain?	1-A very short time	2-A medium amount	3-Almost all the time
How much pain did you feel?	1-A little	2- A medium amount	3- Very tired
How much did the pain bother you or trouble you?	0-Not at all	1-A little	2- A medium amount	3- Very much

5. Did you feel worried yesterday or today?
YES or NO
If YES:

How much of the time did you feel worried?	1-A very short time	2-A medium amount	3-Almost all the time
How worried did you feel?	1-A little	2- A medium amount	3- Very tired
How much did feeling worried bother you or trouble you?	0-Not at all	1-A little	2- A medium amount	3- Very much

6. Did you feel like eating yesterday or today as you normally do?

YES or NO

If YES:

How long did this last?	1-A very short time	2-A medium amount	3-Almost all the time

How much did this bother you or trouble you?	0-Not at all	1-A little	2- A medium amount	3- Very much

7. Did you feel like you were going to vomit (or going to throw up) yesterday or today?

YES or NO

If YES:

How much of the time did you feel like you could vomit (or throw up)?	1-A very short time	2-A medium amount	3-Almost all the time

How much did this feeling bother you or trouble you?	0-Not at all	1-A little	2- A medium amount	3- Very much

8. Did you have trouble going to sleep the last 2 nights?

YES or NO

If YES:

How much did not being able to sleep bother you or trouble you?	0-Not at all	1-A little	2- A medium amount	3- Very much

Other:

9. If you had anything else which made you feel bad or sick yesterday or today, write it here*:

*_____

_____

If YES:

How much did this bother you or trouble you?	0-Not at all	1-A little	2- A medium amount	3- Very much

10. If you had anything else which made you feel bad or sick yesterday or today, write it here*:

*_____

_____

If YES:

How much did this bother you or trouble you?	0-Not at all	1-A little	2- A medium amount	3- Very much

APPENDIX 2

1. Did you feel like you were going to vomit (or going to throw up) yesterday or today?

YES or NO

If so, how much did you feel like you could vomit (or could throw up)? Please put a mark on the line

Not at all |_____| Almost all the time

2. How sad have you been feeling in the last 2 days? Please put a mark on the line

Not at all |_____| Almost all the time

3. During the past 2 days how has your body been feeling? Please put a mark on the line

Not at all |_____| Almost all the time

4. PAIN SCALE: Mark on the line below how much pain you had during the past 2 days.

Not at all |_____| Almost all the time

Reprinted from J Pain Symptom Manage 23(1). Collins, J. J. , T. D. Devine, et al. *The measurement of symptoms in young chiildren with cancer: the validation of the Memorial Symptom Assessment Scale in children aged 7-12.* Pages 10-16. Copyright (2002).

MSAS (13-18)

Section 1

Instructions: We have listed 23 symptoms below. Read each one carefully. If you have had the symptom during this past week, circle **YES**. If **YES**, let us know how **OFTEN** you had it, how **SEVERE** it was usually, and how much it **BOTHERED OR DISTRESSED** by circling the appropriate answer. If you **DID NOT HAVE** the symptom circle **NO**.

DURING THE PAST WEEK DID YOU HAVE ANY:

1. DIFFICULTY CONCENTRATING or PAYING ATTENTION?

YES or NO

If YES:

How often did you have it?	1- Almost never	2- Sometimes	3- A lot	4- Almost always
How severe was it usually?	1- Slight	2- Moderately	3- Severe	4- Very severe

How much did it bother you or distresss you?	0-Not at all	1- A little bit	2- Somewhat	3- Quite a bit	3- Very much

2. PAIN?

YES or NO

If YES:

How often did you have it?	1- Almost never	2- Sometimes	3- A lot	4- Almost always
How severe was it usually?	1- Slight	2- Moderately	3- Severe	4- Very severe

How much did it bother you or distresss you?	0-Not at all	1- A little bit	2- Somewhat	3- Quite a bit	3- Very much

3. LACK OF ENERGY?

YES or NO

If YES:

How often did you have it?	1- Almost never	2- Sometimes	3- A lot	4- Almost always
How severe was it usually?	1- Slight	2- Moderately	3- Severe	4- Very severe

How much did it bother you or distresss you?	0-Not at all	1- A little bit	2- Somewhat	3- Quite a bit	3- Very much

4. COUGH?

YES or NO

If YES:

How often did you have it?	1- Almost never	2- Sometimes	3- A lot	4- Almost always
How severe was it usually?	1- Slight	2- Moderately	3- Severe	4- Very severe

How much did it bother you or distresss you?	0-Not at all	1- A little bit	2- Somewhat	3- Quite a bit	3- Very much

5. FEELING OF BEING NERVOUS?

YES or NO

If YES:

How often did you have it?	1- Almost never	2- Sometimes	3- A lot	4- Almost always
How severe was it usually?	1- Slight	2- Moderately	3- Severe	4- Very severe

How much did it bother you or distresss you?	0-Not at all	1- A little bit	2- Somewhat	3- Quite a bit	3- Very much

6. DRY MOUTH?

YES or NO

If YES:

How often did you have it?	1- Almost never	2- Sometimes	3- A lot	4- Almost always
How severe was it usually?	1- Slight	2- Moderately	3- Severe	4- Very severe

How much did it bother you or distresss you?	0-Not at all	1- A little bit	2- Somewhat	3- Quite a bit	3- Very much

7. NAUSEA or FEELING LIKE YOU COULD VOMIT?

YES or NO

If YES:

How often did you have it?	1- Almost never	2- Sometimes	3- A lot	4- Almost always
How severe was it usually?	1- Slight	2- Moderately	3- Severe	4- Very severe

How much did it bother you or distresss you?	0-Not at all	1- A little bit	2- Somewhat	3- Quite a bit	3- Very much

8. A FEELING OF BEING DROWSY?

YES or NO

If YES:

How often did you have it?	1- Almost never	2- Sometimes	3- A lot	4- Almost always
How severe was it usually?	1- Slight	2- Moderately	3- Severe	4- Very severe

How much did it bother you or distresss you?	0-Not at all	1- A little bit	2- Somewhat	3- Quite a bit	3- Very much

9. NUMBNESS/TINGLING or PINS AND NEEDLES FEELING IN HANDS or FEET?

YES or NO

If YES:

How often did you have it?	1- Almost never	2- Sometimes	3- A lot	4- Almost always
How severe was it usually?	1- Slight	2- Moderately	3- Severe	4- Very severe

How much did it bother you or distresss you?	0-Not at all	1- A little bit	2- Somewhat	3- Quite a bit	3- Very much

10. DIFFICULTY SLEEPING?

YES or NO

If YES:

How often did you have it?	1- Almost never	2- Sometimes	3- A lot	4- Almost always
How severe was it usually?	1- Slight	2- Moderately	3- Severe	4- Very severe

How much did it bother you or distresss you?	0-Not at all	1- A little bit	2- Somewhat	3- Quite a bit	3- Very much

11. PROBLEMS WITH URINATION or 'PEEING'?

YES or NO

If YES:

How often did you have it?	1- Almost never	2- Sometimes	3- A lot	4- Almost always
How severe was it usually?	1- Slight	2- Moderately	3- Severe	4- Very severe

How much did it bother you or distresss you?	0-Not at all	1- A little bit	2- Somewhat	3- Quite a bit	3- Very much

12. VOMITING OR THROWING UP?

YES or NO

If YES:

How often did you have it?	1- Almost never	2- Sometimes	3- A lot	4- Almost always
How severe was it usually?	1- Slight	2- Moderately	3- Severe	4- Very severe

How much did it bother you or distresss you?	0-Not at all	1- A little bit	2- Somewhat	3- Quite a bit	3- Very much

13. SHORTNESS OF BREATH?

YES or NO

If YES:

How often did you have it?	1- Almost never	2- Sometimes	3- A lot	4- Almost always
How severe was it usually?	1- Slight	2- Moderately	3- Severe	4- Very severe

How much did it bother you or distresss you?	0-Not at all	1- A little bit	2- Somewhat	3- Quite a bit	3- Very much

14. DIARRHEA OR LOOSE BOWEL MOVEMENTS?

YES or NO

If YES:

How often did you have it?	1- Almost never	2- Sometimes	3- A lot	4- Almost always
How severe was it usually?	1- Slight	2- Moderately	3- Severe	4- Very severe

How much did it bother you or distresss you?	0-Not at all	1- A little bit	2- Somewhat	3- Quite a bit	3- Very much

15. FEELINGS OF SADNESS?

YES or NO

If YES:

How often did you have it?	1- Almost never	2- Sometimes	3- A lot	4- Almost always
How severe was it usually?	1- Slight	2- Moderately	3- Severe	4- Very severe

How much did it bother you or distresss you?	0-Not at all	1- A little bit	2- Somewhat	3- Quite a bit	3- Very much

16. SWEATS?

YES or NO

If YES:

How often did you have it?	1- Almost never	2- Sometimes	3- A lot	4- Almost always
How severe was it usually?	1- Slight	2- Moderately	3- Severe	4- Very severe

How much did it bother you or distresss you?	0-Not at all	1- A little bit	2- Somewhat	3- Quite a bit	3- Very much

17. WORRYING?

YES or NO

If YES:

How often did you have it?	1- Almost never	2- Sometimes	3- A lot	4- Almost always
How severe was it usually?	1- Slight	2- Moderately	3- Severe	4- Very severe

How much did it bother you or distresss you?	0-Not at all	1- A little bit	2- Somewhat	3- Quite a bit	3- Very much

18. ITCHING?

YES or NO

If YES:

How often did you have it?	1- Almost never	2- Sometimes	3- A lot	4- Almost always
How severe was it usually?	1- Slight	2- Moderately	3- Severe	4- Very severe

How much did it bother you or distresss you?	0-Not at all	1- A little bit	2- Somewhat	3- Quite a bit	3- Very much

19. LACK OF APPETITE or NOT WANTING TO EAT?

YES or NO

If YES:

How often did you have it?	1- Almost never	2- Sometimes	3- A lot	4- Almost always
How severe was it usually?	1- Slight	2- Moderately	3- Severe	4- Very severe

How much did it bother you or distresss you?	0-Not at all	1- A little bit	2- Somewhat	3- Quite a bit	3- Very much

20. DIZZINESS?

YES or NO

If YES:

How often did you have it?	1- Almost never	2- Sometimes	3- A lot	4- Almost always
How severe was it usually?	1- Slight	2- Moderately	3- Severe	4- Very severe

How much did it bother you or distresss you?	0-Not at all	1- A little bit	2- Somewhat	3- Quite a bit	3- Very much

21. DIFFICULTY SWALLOWING?

YES or NO

If YES:

How often did you have it?	1- Almost never	2- Sometimes	3- A lot	4- Almost always
How severe was it usually?	1- Slight	2- Moderately	3- Severe	4- Very severe

How much did it bother you or distresss you?	0-Not at all	1- A little bit	2- Somewhat	3- Quite a bit	3- Very much

22. FEELINGS OF BEING IRRITABLE?

YES or NO

If YES:

How often did you have it?	1- Almost never	2- Sometimes	3- A lot	4- Almost always
How severe was it usually?	1- Slight	2- Moderately	3- Severe	4- Very severe

How much did it bother you or distresss you?	0-Not at all	1- A little bit	2- Somewhat	3- Quite a bit	3- Very much

23. HEADACHE?

YES or NO

If YES:

How often did you have it?	1- Almost never	2- Sometimes	3- A lot	4- Almost always
How severe was it usually?	1- Slight	2- Moderately	3- Severe	4- Very severe

How much did it bother you or distresss you?	0-Not at all	1- A little bit	2- Somewhat	3- Quite a bit	3- Very much

SECTION 2

Instructions: We have listed 8 symptoms below. Read each one carefully. If you have had the symptom during this past week, let us know how SEVERE it was usually, and how much it BOTHERED OR DISTRESSED by circling the appropriate answer. If you DID NOT HAVE the symptom circle No.

DURING THE PAST WEEK DID YOU HAVE ANY:

1. MOUTH SORES?

YES or NO

If YES:

How severe was it usually?	1- Slight	2- Moderately	3- Severe	4- Very severe

How much did it bother you or distresss you?	0-Not at all	1- A little bit	2- Somewhat	3- Quite a bit	3- Very much

2. CHANGE IN THE WAY FOOD TASTES?

YES or NO

If YES:

How severe was it usually?	1- Slight	2- Moderately	3- Severe	4- Very severe

How much did it bother you or distresss you?	0-Not at all	1- A little bit	2- Somewhat	3- Quite a bit	3- Very much

3. WEIGHT LOSS?

YES or NO

If YES:

How severe was it usually?	1- Slight	2- Moderately	3- Severe	4- Very severe

How much did it bother you or distresss you?	0-Not at all	1- A little bit	2- Somewhat	3- Quite a bit	3- Very much

4. HAIR LOSS?

YES or NO

If YES:

How severe was it usually?	1- Slight	2- Moderately	3- Severe	4- Very severe

How much did it bother you or distresss you?	0-Not at all	1- A little bit	2- Somewhat	3- Quite a bit	3- Very much

5. CONSTIPATION or FEELING UNCOMFORTABLE BECAUSE BOWEL MOVEMENTS ARE LESS OFTEN?

YES or NO

If YES:

How severe was it usually?	1- Slight	2- Moderately	3- Severe	4- Very severe

How much did it bother you or distresss you?	0-Not at all	1- A little bit	2- Somewhat	3- Quite a bit	3- Very much

6. SWELLING OF ARMS AND LEGS?

YES or NO

If YES:

How severe was it usually?	1- Slight	2- Moderately	3- Severe	4- Very severe

How much did it bother you or distresss you?	0-Not at all	1- A little bit	2- Somewhat	3- Quite a bit	3- Very much

7. 'I DON'T LOOK LIKE MYSELF'?

YES or NO

If YES:

How severe was it usually?	1- Slight	2- Moderately	3- Severe	4- Very severe

How much did it bother you or distresss you?	0-Not at all	1- A little bit	2- Somewhat	3- Quite a bit	3- Very much

8. CHANGES IN SKIN?

YES or NO

If YES:

How severe was it usually?	1- Slight	2- Moderately	3- Severe	4- Very severe

How much did it bother you or distresss you?	0-Not at all	1- A little bit	2- Somewhat	3- Quite a bit	3- Very much

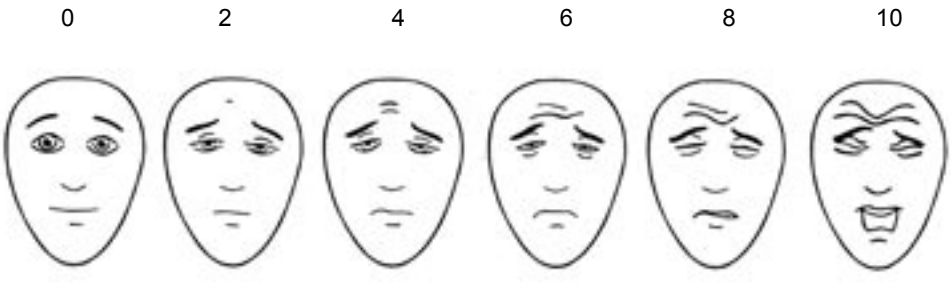
Reproduced with permission. Collins, J. J., M. E. Byrnes, et al. (2000). J Pain Symptom Manage 19(5): 363-77.

FACES PAIN SCALE-REVISED (FPS-R)

Spanish Instructions:	English Instructions:	French Instructions:
Pregúntele al niño qué nombre le da al "dolor" y use ese mismo término a lo largo de esta evaluación. "Estas caras muestran cuánto algo puede doler. Esta cara [señale la cara del extremo izquierdo] indica que no hay nada de dolor. Las caras van mostrando más y más dolor [señale cada una de izquierda a derecha] hasta llegar a ésta [señale la cara del extremo derecho] – que muestra muchísimo dolor. Señala la cara que indique cuánto dolor tienes [ahora]." Asigne un score a la cara seleccionada por el niño, contando de izquierda a derecha 0, 2, 4, 6, 8, o 10, de manera que '0' = 'ausencia de dolor' y '10' = 'muchísimo dolor.' No use palabras como 'contento' o 'triste'. La intención de esta escala es medir como el niño se siente en su interior, no como luce su rostro.	In the following instructions, say "hurt" or "pain", whichever seems right for a particular child. "These faces show how much something can hurt. This face (point to left-most face) shows no pain. The faces show more and more pain (point to each from left to right) up to this one (point to the right-most face) — it shows very much pain. Point to the face that shows how much you hurt [right now]." Score the chosen face 0, 2, 4, 6, 8, or 10, counting left to right, so '0'='no pain' and '10' = 'very much pain'. Do not use words like 'happy' and 'sad'. This scale is intended to measure how children feel inside, not how their face looks.	"Ces visages montrent combien on peut avoir mal. Ce visage (montrer celui de gauche) montre quelqu'un qui n'a pas mal du tout. Ces visages (les montrer un à un de gauche à droite) montrent quelqu'un qui a de plus en plus mal, jusqu'à celui-ci (montrer celui de droite), qui montre quelqu'un qui a très très mal. Montre-moi le visage qui montre combien tu as mal en ce moment. " Les scores sont de gauche à droite: 0, 2, 4, 6, 8, 10. '0' correspond donc à 'pas mal du tout' et '10' correspond à 'très très mal.' Remarques: Exprimez clairement les limites extrêmes: "pas mal du tout" et "très très mal" N'utilisez pas les mots 'triste' ou 'heureux' Précisez bien qu'il s'agit de la sensation intérieure, pas de l'aspect affiché de leur visage. "Montre-moi comment tu te sens à l'intérieur de toi."

Hicks CL, von Baeyer CL, Spafford P, van Korlaar I, Goodenough, B. The Faces Pain Scale – Revised: Toward a common metric in pediatric pain measurement. Pain 2001; 93:173-183. Scale adapted from: Bieri D, Reeve R, Champion G, Addicoat L, Ziegler J. The Faces Pain Scale for the self-assessment of the severity of pain experienced by children: Development, initial validation and preliminary investigation for ratio scale properties. Pain 1990;41:139-150. Copyright 2001 International Association for the Study of Pain (IASP). May be photocopied for clinical and research use. For all other uses including republication, permission should be sought from IASP. For further information and translations into other languages see www.painsourcebook.ca .

Fold here/ Doble aquí/ Plier



15 Care of the Elderly in Developing Countries

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DIFFERENCES BETWEEN THE DEVELOPED AND DEVELOPING WORLD

A major epidemiological finding about the world population in the 20th century was the considerable increase in the number of older people in both developed and developing countries (1,2). This trend is expected to continue into the future. Table 1, below, summarizes some key demographic changes that have modified the health priorities of developing countries. In fact, social and economic transformations of the last few decades have contributed to the emergence of a new set of health care priorities which include cardiovascular diseases, cancer, cirrhosis, diabetes, chronic obstructive pulmonary diseases and injuries. The main causes of mortality in developing countries are similar to those found in the developed world. While the prevalence of infectious diseases in developing countries has decreased sharply, there has been an increase in the relative importance of chronic incurable diseases with an almost identical profile to that found in Western Europe, North America and Japan (1). This is mainly due to the aging of the population, a decline in fertility, an increase in life expectancy, rapid urbanization and industrialization, changes in life styles, and a relatively improved access to healthcare. Unfortunately, a timely improvement in the treatment of disease and in the development of palliative care has not occurred. In the vast majority of developing countries, it is particularly common for elderly persons to be consistently affected by endemic poverty, poor diet, isolation, ill health and inadequate housing. Table 2, summarizes the principal diseases affecting the elderly population that may also require palliative care.

Table 1. Epidemiological facts related to ageing population.

- Of the 600 million elderly people (≥ 60 years) living in the world today, approximately 360 million live in developing countries.
- By 2020, the proportion of the population over 60 years will be 12% in Latin America, 17% in East Asia and 23% in Europe and North America.
- By 2020, approximately 75% of all deaths in developing countries will be age related: cardiovascular, cancer, chronic obstructive pulmonary diseases, cirrhosis and diabetes.

Data summarized from the 2002 WHO Fact Sheets (1).

There are major differences between elderly patients, diagnosed with cancer, in developed and developing countries as shown in Table 3. These differences have common roots in poverty, insufficient health care access, and the absence of efficient social and political support. There are two major differences in these societies. They are related to the natural history of chronic diseases and the characteristics of medical education and socio-cultural issues. Medical education about the needs of the elderly patient is generally limited in developing countries, and furthermore, palliative care is not a priority of national health policies. Another problem for the elderly population in developing countries is the lack of social and financial support. This is aggravated by the progressive deterioration of family ties, and responsibilities, for the care of its eldest members.

Table 2. Advanced chronic non-neoplastic diseases* that require palliative care.

- Chronic Obstructive Pulmonary Disease.
- Chronic Heart Failure.
- Degenerative Diseases of the Central Nervous System:
    - Cerebrovascular diseases.
    - Dementias: Alzheimer, Vascular.
    - Parkinson's disease.
- Chronic Liver Failure: chronic encephalopathy – intractable ascites.
- Chronic Renal Insufficiency.
- Acquired Immunodeficiency Syndrome (AIDS).
- Osteoarthritis Fractures and Immobilization

*Cachexia is a common syndrome present in end-stage, chronic non-neoplastic diseases.

CANCER IN THE ELDERLY

Cancer is primarily a disease of the elderly. Many older patients are treated in community hospitals where anticancer therapies are unlikely to be given and where palliation of symptoms should be of primary importance. The diagnosis of cancer is usually made at late stages when the disease has already disseminated. It is estimated that 70% of all cancer deaths occur in individuals 65 years and older. Because of poor access to appropriate treatment in developing countries, approximately 60% of cancer patients have incurable metastatic disease at the time of diagnosis.

Optimally, patients with cancer should be managed by an experienced multidisciplinary healthcare team, as is the case in developed countries. However, comprehensive cancer centers are rarely found in developing countries. Cancer patients in developing countries face many barriers to palliative care. These barriers are due to inadequate education of health practitioners, attitudes of the patients, the makeup of the health care system, and the fact that by the time the diagnosis of cancer is made the disease is usually very advanced. Palliative care education must be provided to health professionals to ensure that all patients, including the elderly, have adequate management of their cancer-related symptoms.

SOCIO-CULTURAL ASPECTS

There are a number of sociological stressors common to all elderly populations, but they are more prevalent and severe in developing countries. The most relevant stressors are:

- *Poor housing, nutrition and unemployment*
- *Frequent abandonment by family members*
- *Poor social security*
- *Extremely limited access to health care and appropriate pharmacotherapy*
- *Physical and mental abuse*
- *Inadequate access to hospice care when needed*
- *A gap between statements of policy makers and concrete actions to improve the care of the elderly*
- *Poor palliative care education of health care professionals*

The number of non-governmental organisations (NGOs) worldwide has increased substantially in the last two decades in developing countries and their influence on health and health care policy has been demonstrated (3). The role of the NGOs as partners in primary health care depends on their commitment to cooperate with the state and business sector, and on their networking capacity. In the event of health-sector reforms, the society should focus on equity and justice, and advocate health as a public responsibility. The impact of such changes may improve health if medical personnel joins forces with NGOs and the civil society. There is a gradual trend towards increasing numbers of individuals involved in the promotion of health for the elderly.

Table 3. Major differences related to cancer among old individuals living in developing and developed countries.

Characteristic	Countries	
	Developing	Developed
Percent of advanced cancer at diagnosis	< 60% advanced stages	> 40% advanced stages
Access to comprehensive cancer treatment	poor	adequate
Cultural constraints for opioid use	common	uncommon
Economic constraints for appropriate drug treatment of pain and other chronic symptoms	major	minor
Adherence to therapy and drug control	scarce	adequate
Multidisciplinary palliative care access	very rare	common
Medical education for the elderly patient	very poor	improving
Number of trained volunteers for care	improving	improving
The elderly patient as a part of the local political agenda	scarce	important

NGOs have increasingly gained quantitative and qualitative importance in the care of poor elderly patients in some developing countries. Religious and non-religious organizations have opened a number of hospices to care for abandoned elderly patients, decreasing substantially the burden to the government's social security system. Appropriate training of volunteers has produced significant improvement in the care of abandoned elderly patients who are confronting a terminal illness either in the domiciliary or hospice settings (3). These organizations have become important in developing countries because they are efficient and provide innovative models that improve care.

ETHICAL ASPECTS

The fundamental moral principles of palliative care for the elderly are the same as those for everyone else. Elderly patients with dementia present specific challenges. In the final stages of dementia, patients are typically unable to walk or feed themselves, incontinent and aphasic, and have lost their capacity to relate to others. Family members, or surrogate decision makers, must make difficult, and often painful, decisions about limiting care. One area of particular concern relates to the provision of tube feeding and hydration. Occasionally, surrogate decision makers for demented patients request tube feeding be given based on the hope of extending life while preventing aspiration pneumonia. Their values and religious beliefs dictate that sustenance must never be withheld - a means to prevent suffering

Recent information supports the conclusion that tube feeding seldom achieves the intended medical benefits, and rather than prevent suffering, it may cause it. Moreover, many secular bioethicists have argued that feeding tubes are not required in patients with advanced dementia and several religious ethicists have come to the same conclusion (4). The families of patients with dementia and feeding difficulties deserve guidance from informed physicians. We believe that physicians should promote hand feeding whenever possible and permit hospice and nursing home regulators to follow their recommendations.

WHAT DIFFERENTIATES THE ELDERLY PATIENT FROM OTHERS RECEIVING PALLIATIVE CARE?

The fundamental issues that characterize the elderly patient are (2):

a) The natural physiological changes due to ageing
b) Declining sensory functions
c) The common coexistence of multiple chronic ailments and polypharmacotherapy
d) Frequent major difficulties in communication related to coexistent dementia, or sensory impairments
e) Differences in pharmacokinetics compared to younger individuals
f) The striking social and economical problems confronting old people in developing countries
g) Insufficient, or inadequate, medical treatment and poor management of pharmacotherapy in developing countries compared to developed countries
h) Major emotional and economical burdens that impact family members and/or surrogates in developing countries compared to developed countries

The Process of Ageing

When the palliative care team is faced with providing care to an elderly patient suffering with a newly diagnosed life limiting illness, the normal processes of ageing must be considered during the development of a treatment plan. The elderly have decreased muscular tissue and a reduced extracellular volume that may increase the chances of dehydration, prerenal failure and nausea which makes it difficult to provide adequate hydration, medication and nutrition using the oral route. Ageing affects the skin making it vulnerable to the development of painful ulcerations and infection in those with reduced mobility secondary to fractures, dementia, Parkinson's disease, and stroke.

Chronic Advanced Organ Failure

- *The presence of chronic advanced organ failure (liver, heart, lungs, kidney, and brain), as well as metastatic cancer, favor the development of prostration and asthenia. The symptoms found in patients with cancer, may also be present in patients with advanced organ failure, such as the anorexia-cachexia syndrome, nausea and vomiting, anxiety and depression.*
- *The coexistence of dementia and delirium; urinary and/or fecal incontinence; the triad of falls – fractures – immobilization; and anxiety or depression make treatment more difficult in the elderly patient with a progressive life limiting illness. It is important to educate family members and caregivers about techniques and methods to prevent complications as well as treatment options. It is also important to rule out a number of reversible conditions that may mimic many of the above symptoms, see Table 4.*

Table 4. Common potentially reversible syndromes in the elderly suffering a progressive life limiting illness.

Syndrome	Pay attention to
Dementia	Deficiency of B_{12}, Hypothyroidism
Depression	Subdural hematoma , Drug overdose
Delirium	Alcohol and benzodiazepines withdrawal syndrome; or caused by digoxin, Haloperidol, opioids, or other drugs
Dehydration	Electrolyte disturbance (diuretic over dose), including hypercalcemia, hypomagnesemia, hyponatremia and inappropriate secretion of antidiuretic hormone.
Urinary incontinence	Infection
Fecal incontinence	Fecaloma, or pseudodiarrhoea
Fractures and bruises	Abuse

Pharmacotherapy

Normal elderly patients, as compared to normal younger patients, usually require a lower dose of medication per kg of body weight. This also pertains to the doses of opioids administered. Particular care is required when prescribing medication for elderly patients who have decreased renal or hepatic function, as well as under nutrition, which is commonly found in developing countries.

- *Doses of medication must be adjusted for the elderly undernourished patient who has a decreased muscular mass, hypoalbuminemia and contraction of the extracellular compartment. In general, a good policy is to initiate any drug by administering one half the normal adult dose.*
- *Characteristically, all phases of pharmacokinetics are slowed as one ages. Therefore doses should not only be decreased, but the time interval between doses must be increased. Since the rate of metabolism of morphine is decreased in the elderly, there is a greater sensitivity of the old, compared to young, individuals to opioids.*
- *Polypharmacotherapy, and self-medication, are particularly common in elderly patients due to the coexistence of chronic ailments and problems with communication.*
- *The problem of self-medication that occurs without the knowledge of physicians and caregivers is a frequent problem in developing countries. Drug interactions and adverse reactions to medications are also a common problems faced by health care professionals, caregivers and family members.*
- *Due to secondary effects, some medications require special attention, particularly in the cognitively impaired. The principal restrictions are found in Table 5 (5).*
- *Whenever possible, the administration of benzodiazepines should be avoided in the elderly. It is wise to remember that older people sleep less, usually 5 – 6 hrs, compared to middle aged individuals. Good substitutes for benzodiazepines used for sleep induction are antihistaminics, haloperidol and thioridazine. If benzodiazepines must be used (i.e. chronic user), it is better to switch to short acting drugs such as lorazepam or alprazolam. If the patient is a chronic user of long-acting benzodiazepines, removal of the drug should be accomplished by slowly reducing doses in small amounts over weeks in order to prevent the appearance of a deprivation syndrome.*
- *There is no pharmacological contraindication for the moderate use of alcoholic beverages in the form of wine, beer or diluted spirits in elderly patients.*

Table 5. Restrictions of drug use in the elderly patient

Always avoid	Restrict use
Barbiturates	Amitriptiline
Flunitrazepam	Methyldopa
Chlorpropamide	Reserpine
Meperidine	Diazepam
Belladona Alkaloids	Chlordiazepoxide
Meprobramate	Carisoprodol
Pentazocine	Cyclobenzaprine
Hyoscyamine	Chlorpheniramine
Propantheline	Promethazine

SYMPTOM CONTROL

In general, the management of symptoms of the elderly is similar to that of younger individuals. It is important to note that community surveys in developed, and developing countries, found that between one third and a one half of older people report falls. If the elderly are to receive appropriate care, and complications are to be avoided, education and counsel are essential for those involved at all levels of their care. Education is particularly important for family caregivers who must implement preventive measures (hygiene, nutrition, prevention of falls, skin and nail care, etc) and also administer drugs for appropriate symptom control. Education and counselling can markedly decrease the suffering experienced by both the patient and family, and it may also reduce the cost of care by preventing complications. This is key in developing countries where economic constraints and insufficient access to adequate medical care are common.

The occurrence, in elderly patients, of incontinence, poor hygiene and amnesia for recent events, combined with chronic illnesses such as heart disease, or cirrhosis, can add to the feelings of guilt, anxiety and personal mortality. The consequences of the loss of bladder or bowel sphincter control can in fact cause embarrassment and fear. Sleep disturbances with apnea episodes, heartburn, and frequency of urination can produce erratic sleep habits that interfere with living a normal life. It is important to remember that loneliness remains the most devastating problem of the elderly. The environment in which elderly persons must live, and navigate, in developing countries is a dimension that is often forgotten by physicians. It is essential to take into consideration how one might alter, or rearrange, aspects of the residence in order to permit older individuals to safely and easily maneuver. Consider the arrangement of rooms in the home, especially the bedroom, bathroom, kitchen, as well as the location of stairs. The provision of assistive devices such as handles and rails can greatly improve access, mobility and the independence of the elderly.

Assessment of Cognitive Function and Depression

Dementia and major depression and delirium are common psychiatric syndromes found in the elderly patients afflicted by cancer and other advanced chronic diseases. Alcoholism is another common coexistent problem that affects approximately 15 % of the elderly patients with psychiatric symptoms and/or cognitive impairment. The most common psychiatric syndrome in the elderly is dementia of varying degrees. Frequently psychotic ideation, of the paranoid type, may coexist with dementia. It has been estimated that approximately 25% of cancer patients will develop mild to major depression. Thirty to fifty percent of patients, age 70 years and older, who suffer with advanced chronic diseases, or cancer, will have some degree of delirium during the course of their illness. Particular attention must be given to the psychiatric differential diagnosis in elderly patients who also have some degree of dementia. Family members can often provide a history of antecedent depression. Frequently, in milder cases of dementia, the patient is aware of their deficiencies in cognitive function and may become depressed. In cases where the diagnosis of depression is in question, a trial with an appropriate antidepressant is indicated. Table 6 summarizes the differential diagnosis for dementia and delirium (6). Clinicians commonly fail to detect dementia in approximately half of affected patients especially during the early course of the disease. Therefore, the palliative care team must proceed with a careful evaluation of cognitive function since this aspect will determine the degree

of autonomy that the elderly patient will have in the near future. This information is critical to the content of the advice given to family members about the care they should provide in areas such as hygiene, nutrition, administration of drugs and the prevention of falls.

Table 6. Differential diagnosis of dementia and delirium

Characteristics	Dementia	Delirium
Onset	Insidious	Sudden
Consciousness	Clear	Reduced
Course	Stable	Fluctuating
Cognition	Altered	Altered
Hallucination	Often absent	Present, visual or auditory
Delusions	Often absent	Present and poorly systematized
Psychomotor activity	Often normal	Variable
Speech	Difficulty in word-finding	Incoherent
Involuntary movements	Often absent	Asterixis – tremor
Organ failure or drug toxicity	Often absent	Both may be present

Modified from Lipowski ZK (6)

One of the best ways for clinicians to perform an initial cognitive assessment is to use the Folstein Mini-Mental Status exam (MMSE) (7) (see chapter 7). This tool contains a series of questions that evaluates memory, language, calculation and orientation. The test has a 30-point scale and is very useful for identifying patients with no impairments as well as those with more severe dysfunction. The test may be administered by appropriately trained personnel and can be administered in less than 10 minutes. MMSE scores under 24 are indicative of significant impairment. Factors unrelated to dementia may lower test scores and may include educational level, depression, mental retardation, and delirium. It is important to emphasize that patients who have an abnormal score on the MMSE may require further neurological evaluation including the evaluation of a B12 and TSH, as outlined in Table 4. Because memory impairment is such a common feature of dementia, another useful tool that can be used during the first visit, or evaluation, is to ask the patient to name three objects, and then have them repeat them after three minutes. Patients who demonstrate difficulty remembering two out of three objects should go on to have a more thorough evaluation.

Undiagnosed depression can mimic dementia; therefore, a thorough full clinical assessment is required in all elderly patients either in the hospital or home setting. An easy way to detect depression in the elderly is to utilize the Yesavage Geriatric Depression Scale (8) or the DSM 4

diagnostic criteria for depression. It is important to always consider the presence of prior alcohol, or benzodiazepine, dependence when analyzing the clinical condition in a symptomatic patient – this is essential for appropriate treatment of anxiety and particularly agitation.

CANCER PAIN (Also see chapter 8)

Cancer is primarily a disease of the elderly. Many older patients are treated in community hospitals where anticancer therapies are unlikely to be given, but where the palliation of symptoms is of primary importance. Pain occurs in approximately 70 per cent of patients with cancer and is the most feared symptom. It is important to recognize that 80 per cent of cancer patients have more than one type of pain. The WHO analgesic ladder is a validated system for treating chronic cancer pain and achieves satisfactory pain relief in the elderly (9). Moderate to severe pain due to cancer, whatever the etiology, usually responds at least partially to opioids. Patients who are overly sensitive to the effects of one opioid may obtain a better response from an alternative opioid. Patients and health care professionals are sometimes deterred from effective opioid use by concerns about addiction (in the form of psychological dependence) and tolerance (because of a fear of loss of clinical effectiveness over time). These concerns are major obstacles to effective pain relief and are unfounded. While physical dependence is a general feature of the use of opioids in chronic pain, psychological dependence is highly unlikely.

Bisphosphonates can reduce bone pain in patients with multiple myeloma, breast and prostate cancer. The administration of epidural or intrathecal opioids, alone or in combination with a local anesthetic, can produce analgesia at very low opioid doses and is accompanied by fewer side effects compared to opioids delivered by other routes (9).

Inadequate pain management is much more prevalent in developing countries because of cultural constraints, insufficient medical and nurse education in palliative care issues and poor access to oral opioid formulations.

It is important to emphasize that elderly patients are less likely than younger patients to receive proper pain management. Elderly patients also are also less likely to take opioids for pain because of attitudes and beliefs of the patient, caregivers or the family members.

Fatigue, dyspnoea, and psychological issues are also important symptoms in the management of elderly cancer patients both during anticancer therapy and near the time of death. Such patients are managed most effectively, as in developed countries, by a multidisciplinary approach using the expertise of a wide range of health care professionals.

It is necessary to apply a multidimensional, interdisciplinary, evaluation using validated scales for activities of daily living, depression and mental status if one wishes to identify problem areas.

Some elderly cancer patients die in the care of a hospice, although many are not referred to this service. There are many barriers to the provision of palliative care to cancer patients and these may be secondary to attitudes and practices of health practitioners, the patients themselves, or

to the health care system of which they are part. It is critically important that educational efforts are focused on health professionals in order to ensure that all patients, including the elderly, have adequate palliation of their cancer-related symptoms.

Chronic Non-Cancer Pain

In 1998, the American Geriatrics Society distributed a set of clinical practice guidelines for the management of chronic pain in older adults (10). These can easily be applied in developing countries. Since then, important advances in pharmacology and strategies for the assessment and management of pain in older persons have emerged. A summary of these recommendations is shown in Table 7, below.

Unfortunately, chronic pain in elderly patients often conjures up negative images and stereotypes associated with longstanding psychiatric problems, futility in treatment, malingering, or drug-seeking behaviour.

Table 7. Recommendations for chronic pain management in the elderly patient

Key issues for appropriate pain control

- Effective treatment of chronic pain lies in comprehensive assessment. All older persons should be screened for persistent pain.
- The verbally administered zero to ten scale or, faces scales, is a good choice for assessment of pain intensity.
- The use of placebos in clinical practice is unethical and there is no place for their use in the management of pain in the elderly patient.
- Acetaminophen should be the first drug to consider in the treatment of mild to moderate pain of skeletal origin.
- Common non-steroidal anti-inflammatory drugs should be avoided in those who require long-term analgesia. The COX-2 inhibitors are preferable. However, these drugs may not be affordable in the public health care system of developing countries.
- Opioids are also effective in older persons with persistent pain. Careful monitoring for the development of adverse side effects is important.
- An individualized program of physiotherapy is essential for skeletal ailments.
- Patient and caregiver education is critical in the management of chronic pain.
- Health care facilities that care for elderly patients should routinely conduct quality control activities to enhance and improve symptom control.

Cognitive Disorders and Depression

The benefits of palliative care are particularly applicable to end-stage dementia patients as well as for patients with other terminal illnesses. Patients with dementia and stroke usually die of medical complications of their disease such as aspiration pneumonia and septic complications due to poor skin care and infected decubitus ulcers. This situation is much worse in developing countries where

there are insufficient numbers of hospices, palliative care programs and well trained individuals in supportive care. Caregivers and health professionals should always be mindful that patients with dementia intermittently are aware of their surroundings. They also may have pain and other symptoms due to complications of the dementia, additional chronic ailments and cancer. Appropriate education of the family, surrogates, and volunteers for the prevention of common complications remains unfulfilled in developing countries.

Dysphagia

Permanent dysphagia is a common symptom in patients with advanced dementia and severe stroke. The problems associated with tube feedings are as important as is the anguish of family, or their surrogates. Of the many decisions that a family, as well as the physician, must make about the care of patients with dementia, none is more heart wrenching than the decision regarding artificial nutrition and hydration.

Many elderly patients do not feel distress from dehydration because they have an impaired thirst mechanism. Under circumstances where the ability to experience thirst is maladaptive, discomfort is minimized, for example during the terminal phase of cancer, irreversible organ failure, Alzheimer's disease and other dementias. Given the weight of the scientific evidence that tube feeding, and gastrostomy tubes, are not effective comfort measures, plus the fact that there is a lack of a compelling ethical argument for their use, we suggest that physicians and hospitals adopt a policy that feeding tubes are not to be used in patients with advanced dementia or severe stroke (10). Hypodermoclysis, the subcutaneous infusion of fluids, is a safe and effective technique for treating dehydration when necessary.

CONCLUSION

There are important generational changes in the developing world that have resulted in an increase need for institutions to care for the elderly. A significant number of elderly patients in developing countries are still cared for by the extended family, as opposed to the care being given by nuclear families in developed countries - this trend is decreasing markedly. A strong, and effective, lobby needs to be directed at policy makers and healthcare organizations, and universities, to promote palliative care programs as well as to increase the number of long-term institutional beds available for effective symptom management with its consequent improvement in the quality of life of terminally ill patients.

Since economic constraints will persist for the foreseeable future, education related to palliative care of the elderly in developing countries should be promoted at all levels of the society. Particular importance should be given to the education of the family on simple methods directed at the care of the elderly, such as hygiene, prevention of falls, symptom control, feeding, dementia and delirium. Support for these programs in developing countries should be a priority for palliative care specialists since non-professionals working in the home will provide most of the care.

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Specific web links

General ageing aspects

http://www.nia.nih.gov/.

http://www.ageing.org/links/index.html.

http://www.stanford.edu/~yesavage/GDS.html

http://www.mednwh.unimelb.edu.au/links.html

Geriatric education and functional assessment tools.

http://www.universityhospital.org/geriatric_education/assessment.html

16 Neurological Disorders

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GENERAL ASPECTS OF NEUROLOGICAL DISORDERS IN DEVELOPING COUNTRIES

Neurological disorders have been acknowledged to play an important role in the disease burden of developing countries accounting for up to 10% of medical admissions in some hospitals (Howlett, personal communication; Winkler, unpublished data). While previously neurological disorders were often included in the vast field of medical disorders, recent developments show a trend in separating them out from the other medical illnesses. In the wider sense however they are inextricably linked with the many tropical diseases showing nervous system involvement. In general, hospital based neurological disorders are more likely to be acute as occurs in central nervous system (CNS) infections, stroke, paralysis and coma. This is in contrast to a large number of chronic neurological disorders that occur at the community level, such as epilepsy, deafness, polio, leprosy, cerebral palsy and others. This chapter deals primarily with aspects of palliative care involving the hospital based group.

The course of the neurological disorders in hospital is variable. Once the nervous system is affected, other organ systems may also be involved more seriously, which may lead to multi-organ failure. Although painting a grim picture in the first instance, a good deal of these patients will leave the hospital, being able to resume normal lives. A classical representative of this group with "curable" neurological involvement is cerebral malaria in which the mortality rate is between 15-20%(1, 2). Less fortunate than the survivors of the acute encephalopathies are those with a progressive course of their neurological disease, who may eventually require palliative care. The cause of disease of many of these patients remains undiagnosed, mainly due to limited resources, especially the lack of neuroimaging and appropriate serology. The physician has to follow the patient's symptoms closely and apply his knowledge of topographic neuroanatomy. Further information may be gained from simple laboratory tests such as thin and thick blood films, hemoglobin, white blood count and erythrocyte sedimentation rate as well as urine and stool analysis. Most laboratories are also able to analyze cerebrospinal fluid and some hospitals offer more sophisticated tests such as VDRL, Widal and HIV. The relatives, a crucial source of information regarding the patient's condition in the Western world, very often are poor historians due to various reasons such as language and culture barriers, but also out of fear of breaking tribal taboos and the wide-spread notion of supernatural powers

having an influence on the course of the disease. Admission to hospital is very often viewed in an ambivalent way, further contributing to withholding vital information and miscommunication between the family and the doctor. Thus, the physician's approach to care is often purely symptom-oriented.

Death and disability are a frequent outcome of neurological patients in developing countries. In an eight-year prospective hospital-based study in Africa involving almost 1600 neurological patients a mortality rate of 28% in hospital was documented (Howlett, personal communication). Infections are among the main cause of mortality with rates over 50%. These infections include bacterial, viral and fungal meningitis, cerebral malaria, CNS tuberculosis, tetanus, and more recently HIV-related infections such as toxoplasmosis and Cryptococcus. Paralysis of any kind is a major cause of hospital admission in developing countries. The main causes of paralysis are stroke, paraplegia, neuropathy, space occupying lesion, neuromuscular and muscle disease. Stroke represents an increasing cause of neurological admissions particularly in urbanized communities in developing countries. In hospital mortality rates of over 40% are not unusual. Paraplegia is also a common cause of neurological disability and mortality (23%). The main causes are trauma, tuberculosis, tumors, and Guillain-Barré syndrome. Community based causes of paraplegia include leprosy, polio, Konzo, lathyrism, tropical ataxic neuropathy and rarely HTLV-1 associated myelopathy. States of coma, confusion and altered level of consciousness are also a common cause of hospital admission. The main causes include infections, metabolic disorders, drugs, overdose, alcohol, space occupying lesions and organ failure. In hospital mortality is often high (66%). Neurodegenerative disorders such as dementia, Parkinson's disease and motor neurone disease are a less common cause of hospital admission and have lower mortality rates (8%).

Based on the authors' experience, neurological palliative care is described against the background of Eastern Africa (Tanzania) where one of the authors (ASW) is currently working as a medical doctor with an interest in neurology. We acknowledge that epidemiology and resources may vary greatly depending on the geographical, socio-economic, and cultural context. Due to the lack of diagnostic means, the classification of neurological disorders in the developing countries requiring palliative care was chosen to be syndrome-based; hence the terms are merely descriptive. Some overlap between the different groups is inevitable, but in most cases allocation of the patient to one of the groups is possible. For each of the different groups the prominent palliative aspects are discussed and treatment strategies are suggested.

MAIN NEUROLOGICAL DISORDERS REQUIRING PALLIATIVE CARE

Infectious Diseases with Involvement of the Central Nervous System

Description of syndrome. These patients present with clear symptoms and signs of meningitis and/or encephalitis. The most important diagnoses are cerebral malaria, bacterial meningitis and tuberculosis (TB) as well as brain abscesses and opportunistic infections in the context of HIV/AIDS, such as toxoplasmosis and cryptococcal meningitis. Other less common infections include trypanosomiasis, schistosomiasis, neurocysticercosis, syphilis, rabies, typhoid fever and rarer tropical infections, the prevalence of which may show geographical variability. The onset is acute especially in cerebral malaria and bacterial meningitis, but may also take a more chronic course such as in tuberculous meningitis and trypanosomiasis. The patient very often is febrile and might

show signs of sepsis. Other organ systems may be involved. Neurological signs are very variable and may range from meningism leading to rapid impairment of consciousness with ensuing coma to a more protracted course reminiscent of dementia, especially in tuberculous meningitis and sleeping sickness. Some patients show signs of diffuse encephalitis, others show focal neurological signs. Seizures may occur. Laboratory tests almost invariably show elevated erythrocyte sedimentation rate and thick blood film may reveal malaria parasites or occasionally trypanosomes. Analysis of cerebrospinal fluid is crucial. If the result is normal and the cause of the disease still obscure special techniques such as the India ink stain may have to be applied. The chest should be examined especially where TB is suspected and anti-TB treatment started in patients whose chest film and/or clinical picture is suggestive of pulmonary TB. The outcome is extremely variable ranging from prompt recovery after appropriate treatment to chronic progression of disease, leading to severe neurological sequelae and/or death.

Palliative treatment. The palliative treatment of end stage encephalopathies caused by infection is that of a stuporous or comatose patient in general. Relatives need to be counseled as to the nature of the symptoms and their presence in a calm environment should be encouraged. Some patients may be restless and agitated before drifting off into coma. In cases with acute delirium, sedation may be required (see below). If pain is a prominent feature, morphine treatment should be initiated in parallel (for details on pain treatment see chapter 8).

Encephalopathies with Focal Neurological Signs

Description of syndrome. These patients present with a history of focal neurological deficit including hemiparesis, ataxia, dysphasia, double vision or other cranial nerve palsies. Numbness, although often present, hardly ever is a main complaint. Some patients present with seizures and other associated neurological signs may only become evident on physical examination. Other patients are brought to the hospital by their relatives because of changes in personality, depression or psychotic episodes, and focal neurological symptoms may go unnoticed in the beginning. The onset may be abrupt as in the context of stroke or more chronic as is the case with cerebral tumors or tuberculomas. There may be a history of heart disease, physical examination may reveal atrial fibrillation and/or a loud heart murmur and the patient may be febrile; the most likely diagnosis here is endocarditis with embolic stroke. Other patients may have high blood pressure pointing towards an ischemic or hemorrhagic event. Patients may complain of chronically ill health, the HIV test may be positive; in this context toxoplasmosis and tuberculomas need to be considered. Intracranial tuberculomas, single or multiple, remain the most important cause of a space occupying lesion in many developing countries (2). Where tuberculosis is suspected, a course of anti-Tb therapy should be started without waiting for histological confirmation. Intracerebral tumors and metastases represent additional causes for focal encephalopathies. A recent history of head injury suggests the possibility of intracranial haematoma. However in most patients, the cause remains unclear and diagnosis is difficult in the absence of neuroimaging. The course of the disease is variable with some patients recovering while others are left with neurological sequelae. Mortality rates are particularly high (see above). Patients may show progressive signs of increasing intracranial pressure, which in the absence of appropriate treatment including neurosurgical intervention will lead to brain herniation and death.

Palliative treatment. Most patients have a fairly rapid course of disease and in the majority of cases relatives are unable to care for the patient at home. What differentiates this group from the others is that the focal cerebral process resulting in a neurological deficit may also act as an epileptogenic focus and, in the case of expanding space occupying lesion, cause signs and symptoms of raised intracranial pressure and coma. Neurological symptoms are thus possible in any combination and need to be treated accordingly (see below). Patients with presumed space occupying lesions (except for bacterial abscesses) may benefit from treatment with steroids, which can prevent seizures and reduce focal neurological symptoms as well as headaches. Steroids may also have a positive effect on the patient's mood and enhance appetite, and are widely available in developing countries. The recommended starting dose of dexamethasone is 12-16 mg once daily in the morning for 5 days, after which the treatment can be discontinued abruptly if no clinical benefit is present, or else tapered down to the lowest possible maintenance dose (can be as low as 2 mg/day).

Seizures at times are intractable in this group. As most of these seizures have a focal origin, phenytoin and carbamazepine are the drugs of choice depending on their availability (dosages see below).

Paraparesis, Quadraparesis and Paralysis Due to Various Causes

This group encompasses diverse disease entities such as spinal cord lesions, motor neurone disease, neuromuscular disorders, myopathies and neuropathies. Paresis/paralysis is present in all of them and its degree will determine the need for palliative care.

Spinal cord lesions resulting in paraparesis/paraplegia are the most frequent disorders in this group: in a prospective study of 900 patients with neurological illnesses in Northern Tanzania, paresis due spinal cord lesion accounted for approximately 100 cases (Winkler, unpublished data). Spinal cord disorders in developing countries are caused by trauma, infections, mainly TB and HIV, or less commonly tumors. Brucellosis and schistosomiasis need to be considered in endemic areas, syphilis should also be borne in mind. Clinically the presence of flaccid and spastic paresis helps to categorize the lesion. Over time patients with spinal cord lesions may develop a sensory level helping further to localize the probable site of the lesion. If there is fever and tenderness of the spine on percussion one should think of the possibility of a spinal cord abscess and give the patients a trial of antibiotics. X-ray examination of the spine and chest is crucial. This may be followed by a trial of anti-Tb drugs in suspected cases.

The term "tropical myeloneuropathies" was used since the 1980's to describe a group of paraparesis of unknown cause (3). Two main clinical entities were distinguished: first, a spastic paraplegia with minimal or no sensory signs, also termed tropical spastic paraparesis; second, a sensory form of ataxia combined with peripheral neuropathy, termed tropical ataxic neuropathy. The causes are mostly nutritional (cassavaism, lathyrism, konzo) (4, 5), a rare cause being HTLV-1 infection.

Poliomyelitis, although on the verge of extinction (in 2000 fewer than 2900 cases worldwide have been reported (2) is still endemic in 20 countries. It needs to be considered in any patient with an acute flaccid paralysis. It may take the course of an acute, often lethal encephalitis with cranial nerve

paralysis or - as in most cases - that of a progressive motor neurone disease. Vaccine associated paralytic poliomyelitis is the most prominent form of the disease not only in the Western countries, but also in the developing world (6, 2). Years after the primary infection, the paresis may deteriorate again due to degeneration of already damaged nerve fibres ("post-polio syndrome").

Motor neurone disease (MND) other than poliomyelitis represents a rare cause for paresis in the tropics. In a large study of tropical illnesses in Nigeria, the incidence in a defined hospital population was found to be 3.5 per 10,000 (7). In a prospective hospital study in Northern Tanzania 28 out of 1593 patients with neurological disorders had motor neurone disease (Howlett, personal communication).

Myopathies are another cause for paresis/paralysis in the tropics. Epidemiological studies on the causes of myopathies in the tropics are lacking. In a sample of 1593 patients with neurological illnesses in Northern Tanzania, 22 cases of myopathy were identified (Howlett, personal communication). Polymyositis is the main cause of myopathy in developing countries. Although muscular dystrophy is not uncommon in Africans, they very rarely present to the hospital unless in very late stages. Children suffering from the disease may be viewed as lazy and thus not brought to medical attention. Other causes for myopathies are myasthenia gravis, although less frequent than in developed countries, and myopathies in the context of Cushing's disease, thyrotoxicosis and hypocalcaemia, amongst others. Many of these conditions are treatable and patients with polymyositis will recover when treated appropriately. However patients with a chronic progressive course of their myopathy may require palliative treatment in advanced stages of their disease.

Palliative treatment: In developing countries, individuals suffering from paraparesis/ quadriparesis are most of the time confined to their beds, as wheelchairs are not readily available in many parts of the world. Many hospitals however have carpenter facilities and crutches of different kinds may be useful to those patients who have got some muscle strength left. As a rule of thumb, the patient needs to be encouraged to spend as much time as possible out of bed and outside the crowded wards where he may contract opportunistic infections. Bedsores and contractures of paretic limbs may be prevented by early mobilization or where not possible passive physiotherapy. Early and regular passive exercise, which in the long run will be undertaken by a relative, will help to relieve pain from increased muscle tone and prevent contractures. Physiotherapists are very often present in midsize rural hospitals and their role in palliative care should not be underestimated. Often a few sessions with the patient and the main carer are enough to teach them some useful physical exercises. In cases where contractures have already developed soft tissue release may be undertaken by a skilled surgeon that may be followed by physiotherapy at some later stage. In patients with spastic paresis baclofen, if available, should be started some days before physiotherapy and continued for as long as possible depending on the side effects and the availability of the drug (for dosage see below).

Bedsores need to be prevented from day one in bedridden patients and nurses should be encouraged to co-operate with the relatives. Frequent changing of the patient's position as well as dry and clean bed sheets are crucial, but unfortunately these simple measures are easily overlooked and action is only taken once bedsores have developed. Bedsores may act as a focus for sepsis which eventually

may take the patient's life. Early catheterization of incontinent patients is also important, as a wet environment will precipitate the development of bedsores. To prevent urinary tract infection a strict sterile approach to catheterization is needed. The use of prophylactic antibiotics is not recommended routinely. In the event of infection antibiotic treatment should be administered according to the result of urine culture and where not available nitrofurantoin is a useful fist line drug. The insertion of suprapubic catheter should be considered early on in palliative care in order to reduce the risk of urethral irritation and infection, encountered frequently in settings with low hygienic standards.

Another important aspect of palliative care in patients with paresis/paralysis is the relief of pain. Pain has multiple origins in these patients. In case of vertebrae destruction, patients may experience severe back pain and/or radicular pain as well as musculoeletal pain. Pain may also result from increased muscle tone and secondary inflammatory and non-inflammatory joint disease. Inactivity over a long time may further lead to painful osteoporosis. In terms of pain relief, simple means need to be exhausted first. They include a hard bed and mattress, frequent changing of position and regular passive exercise as well as massages of painful body parts. In terms of medication the WHO ladder (see chapter 3) should be adhered to. Most hospitals in the developing countries have paracetamol and some non-steroidal anti-inflammatory drugs such as ibuprofen and indomethacin, as well as morphine sulphate. Diazepam can be added in small doses wherever muscular pain is present, although the dose has to be titrated between pain relief and remaining muscle strength. Amitriptyline 25-50 mg nocté or carbamazepine 200 mg three times daily may be tried in patients with a neuropathic component (shooting, tingling or burning pain). Where muscle cramps are present, quinine sulphate, which is widely available, should be tried in doses of 200 mg twice daily.

Chronic Encephalopathies

Description of the syndrome. These patients present with chronic progressive intellectual decline, intermittent confusion and changes in personality, the latter usually being the cause for hospital admission. Many of these patients complain of chronically ill health over some time. Social history may reveal regular and heavy alcohol consumption and an unsteady life style. Patients may be dishevelled and malnourished, and some may have been abandoned by their families. Past history may reveal head trauma. The most prominent features are memory impairment, changes in personality and intermittent confusion. There may be signs of diffuse encephalopathy such as frontal release signs, increased reflexes, ataxia and incontinence. Parkinsonism or other extrapyramidal signs may be present. Behavioral and psychiatric disturbances such as depression and/or psychosis are common, while seizures are not. There may be hypertension in the elderly; an HIV test is indispensable in the younger population. Laboratory tests are usually normal or negative and organ failure excluded. Low hemoglobin should prompt treatment with vitamin B12 and patients with a positive alcohol history should be given high doses of thiamine. Malnourished patients with additional dermatitis need to be given nicotinic acid. Patients with signs of hypothyroid disease may be given a trial of thyroxin where available. The possibility of a brain tumor, especially meningioma, needs also to be considered. Chronic CNS infections such as syphilis and tuberculosis should be borne in mind.

Palliative treatment. Most chronic encephalopathies are progressive and the patients may be in and out of hospital several times. Counseling of relatives as to the nature of the disease is important and co-operation needs to be encouraged. Due to the protracted course of disease many families prefer to care for the patient at home out of financial considerations, thus palliative treatment needs to extend beyond hospital borders. Regular home visiting by trained nursing staff may be an option, but is often unrealistic. An alternative is to choose one relative as an intermediary who comes back to hospital at regular intervals without the patient to give feedback on the patient's condition, receive medical advice and stock up on needed medication. This can save resources on both sides.

Owing to the protracted nature of the neurological disorder, patients may succumb to opportunistic infections such as pneumonia leading to sepsis or pulmonary emboli with cardiac arrest. Although the ultimate cause of death may be non-neurological, during the long course of disease the full gamut of neurological and psychiatric symptoms such as acute confusion, depression, sleep disturbances, hallucinations, agitation and other behavioral problems, impairment of communication, dysphasia, increased muscle tone and pains of multiple origins may be encountered. How to treat each of these symptoms is summarized below. Special mentioning needs to be made of medical problems ensuing from the patient being bedridden for a long time such as bedsores and contractures (see above under point 3).

Acute and Subacute Encephalopathies of Obscure Cause

Description of syndrome. These patients present with a relatively short history of intermittent confusion and decline in mental capacities. On examination there are variable non-localizing neurological signs. These include increased muscle tone and reflexes, frontal release signs such a positive snout and/or palmomental reflexes, gait ataxia and incontinence amongst others. Seizures are usually not present. Patients are typically afebrile and other organ systems are not involved. There is no sign pointing towards an infectious cause or a focal cerebral lesion and therefore the term encephalopathy of obscure cause seems to be appropriate. Additional laboratory tests such as thick blood film for malaria parasites, VDRL, Widal and HIV tests are negative. The erythrocyte sedimentation rate is usually normal. The disease is rapidly progressive and patients very often become unmanageable in the ward. Behavioral and psychiatric symptoms become prominent and the patients may be bedridden early in the course of the disease. It is difficult to speculate on possible causes. Patients and relatives often deny a history of excessive alcohol abuse, thus Wernicke encephalopathy may not be recognized as such. Another possibility is poisoning due to the intake of "mitishamba" i.e. local herbs, some of which have clearly been shown to cause intravasal haemolysis and acute renal failure; neurotoxic mechanisms may also be involved. In most cases the cause of the disease will remain obscure. In a curative attempt, all of these patients should be given antimalaria treatment, as typical signs of malaria may be absent due to prior intake of drugs in the dispensaries. There is the possibility, although rare, of blood slide negative cerebral malaria. Patients should also be given a trial of thiamine and vitamin B12 irrespective of whether they are anemic or not. Unfortunately most of these patients will not recover. The course of disease is rapidly progressive leading to altered level of consciousness and coma. The majority of the patients die in hospital before the relatives are able to make necessary arrangements to take them home.

Palliative treatment. The major palliative problems here are psychiatric and behavioral. The patients very often are anxious, fidgety and agitated; their actions are unpredictable causing major management problems in the ward. In developing countries there is little tolerance towards aggressive individuals. Patients very often are restrained and dragged to the nearest dispensary or hospital, where the doctor meets a fearful and confused patient. Their bodies are covered with marks that bear witness of infliction of various ritualistic procedures in an attempt to calm down the patient. Even "westernised" nursing staff may resort to such drastic measures in situations of extreme crisis. Relatives as well as nurses need to be counseled as to the nature of the disease. If possible the patients should be put in smaller rooms where there is less stimulation from other patients. Antipsychotic and/or anxiolytic treatment should be started when first signs of an anxiety or agitation are evident. It is important to have sufficient supplies of i.m/iv. preparations, as most of these patients are not co-operative. Haloperidol, chlorpromazine and diazepam are widely available in developing countries (for dosage see Table 2).

MAIN NEUROLOGICAL SYMPTOMS IN PALLIATIVE CARE

(Note: for recommendations on pain management see chapter 8)

Acute Confusional State (Delirium)

The causes of delirium are extremely variable – basically, anything which affects the central nervous system can lead to confusion and delirium. The main causes are summarised in Table 1.

Table 1: Causes of confusion/delirium	
Metabolic	Infections, dehydration, hypoxia/hypercapnia, hypo/hyperglycaemia, hypercalcaemia, renal or liver failure
Drugs/toxic substances and their withdrawal	Alcohol, anticholinergics, opioids, benzodiazepines, barbiturates, anticonvulsants, steroids, antibiotics, organophosphates (suicide attempt), chloroquine, local herbs Withdrawal: Alcohol, nicotine, opioids, benzodiazepines, barbiturates
Physical	Pain, fever, fatigue, trauma, stroke, infections
Psycho-social	Change of environment (esp. in demented patients), anxiety, depression, psychosis, catatonia, hysteria
Spiritual	Death anxiety
Terminal	Terminal organ failure, circulatory collapse, shock, direct disease effect on/involvement of the CNS

Treatment of delirium depends on the clinical situation and the therapeutic goal. Even in the palliative setting, up to half of all episodes of delirium may be reversible(8), while the rest heralds the beginning of the dying phase. If the patient is clinically in the dying phase, treatment is purely symptomatic, beginning with haloperidol (Table 2). At earlier stages, the search for treatable causes is pre-eminent, followed by the installment of non-pharmacological measures and thereafter the initiation of drug treatment. In cases of treatment-refractory delirium, terminal sedation may become necessary.

Table 2: Therapy of delirium
1. Treat reversible causes if possible (Table 1)
2. General supportive measures – light, reassurance, touch, music
3. Explain situation to staff and family
4. Calm presence of staff and family members
5. Potent neuroleptics, e.g. Haloperidol: 1.5-3 mg p.o. (repeat after 1 hr if necessary), s.c. bolus 2.5 – 10 mg, s.c. infusion 5-30 mg over 24 h Chlorpromazine: 25-50 mg i.m. or 100-200 mg p.o.
6. Benzodiazepines, if anxiety, high seizure risk (only in addition to neuroleptics) Diazepam: 10-20mg (p.o., rectally), or Lorazepam: 0,5-2 mg (p.o., s.l., i.m., i.v.), or Midazolam: 5-20 mg (i.v., s.c.)

Behavioral/Psychiatric Disturbances

Most patients with neurological disorders involving the CNS (with the exception of MND patients) will at some point show behavioral disturbances which may manifest as loss of orientation, impairment of cognition and memory, affective disinhibition, social withdrawal, or aggressiveness. These changes can profoundly affect the patients' social environment, and lead to a disruption of their social support systems. The way families and social groups deal with such changes is very variable. Sometimes they may be attributed to "evil spirits" inhabiting the patient, which can lead to social and familial ostracism. This type of causal attribution also leads to very late presentation of the patients in the hospital, since the somatic nature of the changes is not recognized. On the other hand, several social systems in the developing world have developed strategies aimed at integrating e.g. elderly demented members of their communities within the resources of the family/community itself.

As a general rule, younger patients usually show more rapid disease progression and more pronounced behavioral changes, which make it difficult for their family/community to adjust. Education about the somatic nature of the disorder may or may not be helpful, depending on the cultural context. In case of aggressive or otherwise dangerous behavior, treatment with haloperidol is indicated (begin as outlined above for delirium, then taper to lowest possible maintenance dose).

Impaired Communication

Impaired communication can be due to impairment of efferent motor structures, such as in MND, dysphasia due to lesions in the dominant hemisphere, or cognitive impairment due e.g. to dementia. In the first case, simple devices such as an alphabet chart or pictograms can be of invaluable help. In all other cases, communication will shift to the non-verbal domain, and the family should be encouraged to try anything which they feel will be acceptable for the patient as a way of communicating. In patients with aphasia, the family should be informed of the somatic nature of the disturbances in speech and understanding. At the same time, the family (and the medical team)

should be cautioned that they should always behave as if the patient understands everything they say. Care must be taken to exclude reversible causes of communication difficulties such as loss of hearing or diminished eyesight.

The effectiveness of communication may depend on the physical comfort of the individual. Appropriate positioning is important to decrease abnormal tone, reduce effort required to maintain a sitting position, minimize reflexive responses and clonus, and optimize respiratory function. General comfort also relies on basic needs being met. People with complex disabilities may rely on care takers to assist them with drinking, toileting, blowing their nose, etc. A quick and efficient method of communicating attention to these tasks should be established for these types of requests and a simple picture communication board at the bedside may be useful.

Impaired speech and language are more difficult to understand when there is background noise and in group settings. Simple listener strategies such as turning off sources of noise such as televisions or radios, shutting doors or moving to a quieter location can make speaking and listening easier. When conversing, seating arrangements should facilitate effective communication; this is best done by ensuring that the participants are sitting facing each other. Adequate lighting and the avoidance of back-lighting the person with communication impairment because this makes it difficult for the listener to read facial expression, supplement intelligibility.

Dysphagia

Dysphagia (difficulty in swallowing) is a frequent syndrome in patients with neurological diseases who need palliative care. The predominant activity limitation in these patients is difficulty in eating and/or drinking safely as well as dependence on tube feeding. Loss of enjoyment of food and drink can severely hamper quality of life. Accordingly, management of dysphagia and of dysphagia-related symptoms is an important part of palliative care. In most patients with severe hypersalivation, anticholinergic drugs (e.g. scopolamine) or drugs with anticholinergic side effects (e.g. amitriptyline) are effective.

Exercises aim to stabilize a patient's condition and to support a safe oral feeding for as long as possible, but should not exhaust the patient. They reinforce the patient's ability to perform the movements necessary for swallowing and to compensate progressive deficits. The choice of exercises to be performed depends on the patient's specific swallowing problem. Examples are lip closure (press the lips together, hold and relax), tonisation of the cheeks (suck the cheeks against the teeth, then hold in that position and relax), mastication (pretend to be chewing on old bread or chewing gum), or tongue movements (try to lick around the lips, to 'count' the teeth, to press the middle part of the tongue against the hard palate, to push the tongue out and pull it back again etc.). Symptoms like hypersalivation, thickening of oral secretions and sudden bouts of coughing are often caused by a reduced swallowing frequency. In those cases, the patient should be encouraged to swallow more often voluntarily.

Dietary modification may help to prevent extremely long mealtimes, fatigue and dread of meals. Soft textures or pureed food can ease oral and pharyngeal transport. Liquids should be thickened when

thin drinks cause choking. Patients and relatives need instruction in the preparation of high caloric food and textures which are easy to chew and swallow (including thickening of liquids in order to avoid dehydration). Triggering of the swallowing reflex can be enhanced by emphasizing taste or temperature.

As dysphagia becomes more severe, augmented feeding techniques such as nasogastric tube feeding and percutaneous endoscopic gastrostomy (PEG) have to be carefully discussed. Nasogastric tube feeding should be only used for a short time because of many disadvantages and PEG is, therefore, in most cases the treatment of choice. In settings with limited resources, urine catheters can be successfully employed for PEG placement. However, care must be taken not to impose a PEG on patients when this is not their wish. The continued delivery of food and fluids may be inappropriate or even deleterious in those patients with very advanced stage disease.

Epileptic Seizures

Epileptic seizures are a common feature of several fatal diseases with CNS involvement. The signs and symptoms of epileptic seizures depend on the brain region involved in the epileptic discharge. Epileptic seizures may occur in a variety of acute syndromes such as tumors, metabolic disorders etc. Seizures are usually self limiting events. During the seizure the patient should be protected against injury and aspiration and observed until full recovery. Antiepileptic drugs will be administered immediately if an increased risk for seizure recurrence is suspected. The most frequently used drugs are shown in Table 3. Phenobarbital is the most widely available antiepileptic drug throughout the developing world. However, where other antiepileptic drugs are in stock, phenobarbital should become second choice due to its sedating properties. If seizures appear under therapy with anticonvulsants, doses should be increased until seizures subside or side effects occur. If seizures persist in spite of maximum tolerable doses of one drug, a change in drug therapy is indicated. Most antiepileptic drugs should be given in smaller doses in the elderly. All antiepileptic drugs need to be withdrawn gradually, especially phenytoin and phenobarbital which have long half-lives.

Almost any type of seizure may become prolonged or repetitive (status epilepticus) and thereby constitute a potentially greater threat than a single seizure. Benzodiazepines such as diazepam are the drugs of choice, characterized by rapid onset of action and relative safety. The initial dose is 10 mg given orally or rectally. An important caveat is that benzodiazepines can cause respiratory depression, especially if given intravenously. The duration of antiepileptic action of diazepam is short, and subsequent administration of an anticonvulsant is necessary, usually phenytoin. Depending on the acuteness of the situation, phenytoin loading can be done rapidly intravenously with up to 25-50mg/min. If phenytoin is not available, a diazepam drip of 100mg/500ml of Glucose 5% can be made up and be given at a starting rate of 0.1 mg/kg/h (beware of cumulation and withdrawal seizures, taper down slowly). If seizures still continue the last option is anesthesia with Thiopental.

Some seizures occur only with specific precipitating factors, such as sleep deprivation and withdrawal of sedatives or alcohol. Treatment aims to avoid these precipitating factors. In the setting of palliative care other factors such as metabolic dysfunction or drug toxicity have to be considered. Furthermore, increase of seizure frequency or induction of status epilepticus can occur in severely ill patients because of inability to swallow medication, vomiting, diarrhea, or confusion.

Table 3: Drug loading and side effects (in the order of their availability)				
Antiepileptic drug	**Starting dose**	**Titration (Usual adult maintenance dose)**	**Side effects**	**Formulation**
Phenobarbital	1. 50 mg p.o. 2. (rapid) 50 mg i.v., s.c. or i.m. every 6 h diluted 1:10 with inj. water 3. (status) 15 mg/kg i.v. diluted 1:10 with inj. water (rate: 100mg/min)	25-50 mg p.o./3 d (long half life) (~50-200 mg/d)	Fatigue, headaches, ataxia, depression, agitation	Oral, i.v., s.c., i.m.
Carbamazepine	200mg	200 mg/3 d (~800-2000 mg/d)	Hyponatraemia, leucopenia, rash, nausea, double vision, ataxia	Oral
Phenytoin	1. 300mg p.o. 2. (rapid) 600mg p.o. for 3 d 3 (status) 1.2-1.5g i.v./24 h	25-50 mg/d (~200-500 mg/d)	Vertigo, rash, leuco-, thrombopenia, fatigue	Oral, i.v. (beware of phlebitis)
Valproate	300 mg p.o.	150-300mg/3d (~ 900-3000 mg/d)	Fatigue, hair loss encephalopathy, nausea, leuco-, thrombopenia	Oral, i.v.

Spasticity

Spasticity, an increased stretch resistance of the passive skeletal muscle with exaggerated tendon jerks, is a common neurological symptom in palliative care resulting from any lesion (e.g. due to a stroke or a brain tumor) of the long corticospinal tract. The overall approach to the management of spasticity includes physical interventions (such as physiotherapy when available, local application of ice) and pharmacotherapy. The aim of the treatment is to prevent joint contractures, bedsores and orthostatic hypotension. Current pharmacological treatment is based on substances that act as muscle relaxants including baclofen and diazepam. Side effects are enhanced muscle weakness and sedation. Both drugs should be started at low dosages (5mg three times daily for baclofen, 2.5 mg twice daily for diazepam) and titrated upwards until a satisfactory symptom relief or unacceptable side effects occur. A combination of the two drugs is only recommended when both monotherapies have failed. It is important to remember that spasticity may be helpful for patients and may compensate for loss of muscle strength. Often, a moderate degree of spasticity is better for the patient than a fully flaccid muscle which may result in inability to walk. Pain resulting from spasticity can be severe, is usually opioid-refractory and needs to be treated with muscle relaxants.

COMMUNICATION, PSYCHOSOCIAL AND SPIRITUAL ASPECTS

Apart from the lack of resources, the most important difference between the developing and the developed world with regards to palliative care is the different attitude towards death itself. The widespread pagan, nature-orientated spiritualism of many tribes throughout the developing world views death and the associated suffering as an inevitable stage of life that the individual has to go through. Spiritual aspects play a major role in the people's attitude towards death. Suffering in many cultures is viewed as a catharsis, a cleansing process that needs to be experienced to make up for the transgression of tribal taboos. Alleviation of such suffering thus is not welcomed.

The attitude towards death however is changing rapidly, strongly influenced by the spread of the religious belief systems throughout the developing world. One core feature of e.g. Christianity is that there is forgiveness of sin, equaling the former transgression of tribal taboos, if the individual is sincerely asking for it in the union with God. In general, adoption of a religious belief will guarantee forgiveness of sins if certain spiritual rules are followed; punishment for former infringements in form of physical suffering has little or no place at all. Palliative care for patients fits the religious spiritual and social system and it is through these new spiritual and social values that caring for the dying has become culturally acceptable, both for the patient and the relatives.

In present day Africa, South America and Asia traditional and religious belief systems co-exist and people may have their own views regarding suffering, disease and death. This needs to be considered when facing a dying patient and his family in the developing world. In this context neurological disorders with their at times demonstrative symptoms such as epileptic seizures are still viewed as something supernatural. People with epileptic seizures very often are thought to be possessed by an evil spirit or to have contracted an ancestral curse. The patient is required to undergo ritualistic procedures in order to get rid of his infliction. Cultural barriers at times make it difficult to deliver appropriate palliative care within this context.

Neurological disorders put particular stress on the social environment of the patient, due to the high incidence of communication impairment and behavioral disturbances. Another obstacle to palliative care of neurological disorders is the chronic course of some of the diseases. This puts financial as well as social strain on the whole family. In developing countries relatives, not nurses, are the primary carers for patients during their stay in hospital. Each patient is required to have at least one relative by their side at all times. Often the hospital is far away from the patient's home which means that in addition to hospital fees food has to be obtained at a much higher price from the local markets. Often the family's financial budget is exhausted prematurely; thus the wish of some families to care for the dying patient at home.

What may be of interest to several parts of the developing world is the concept of "positive deviance". According to this concept, in order to effectively help a population to reach a definite goal (e.g. better care of the dying) in a developing environment, the teaching of strategies developed in industrialized countries is often not helpful. Rather, a careful field observation should be conducted in order to pinpoint those cases in which a particularly good achievement of the goal has been observed within the local community (e.g., families or communities which have developed particularly good

ways of dealing with their elderly and dying members). These strategies should be carefully analyzed and then spread out to the neighboring communities – their coming from within, rather than outside, the local system will usually increase acceptance and penetrance, and therefore lead to a larger and faster improvement with regard to the intended goal. To our knowledge, this model has not yet been studied in the field of palliative care in the developing world. Given its flexibility, it may be applicable to every step of life-threatening illnesses, from the delivery of the diagnosis all the way through death and bereavement.

USEFUL CONSIDERATIONS FOR PALLIATIVE CARE OF NEUROLOGICAL ILLNESSES IN DEVELOPING COUNTRIES

Palliative care in developing countries needs to be provided towards the background of lack of resources, rendering diagnoses and treatment difficult, as well as different spiritual, social and cultural values. Based on the above the approach to palliative care in developing countries is different and the points below should be taken into consideration when caring for the terminally ill neurological patient:

1. *Over a quarter of patients admitted with neurological disorders die in hospital.*
2. *Facilities for home care or hospice provision are scarce.*
3. *Family members are the main carers.*
4. *In the developed countries most patients have been given a definite neurological diagnosis and palliative care is provided for neurological disorders known to be terminal. In the developing world, palliative care very often is given along with curative treatment for a presumptive clinical diagnosis. In order to implement palliative care the carers have to accept that the patient is dying. This may be medically and culturally unacceptable in many clinical cases.*
5. *Many patients with a more chronic course of their disease such as paraplegia or neurodegenerative diseases are taken home at the request of their families out of financial considerations.*
6. *Simple and affordable measures need to be emphasized. They include early prevention of bedsores, maintenance of acceptable standard of hygiene, use of bed nets to prevent malaria, attention to nutrition and directly observed medication amongst others.*
7. *Access to and sufficient supply of morphine is crucial (9).*
8. *Professional access to information and education needs to be reinforced.*
9. *Spiritual and cultural values need to be acknowledged and decisions made by the patient and their relatives based on these values have to be accepted.*
10. *The concept of positive deviance should be borne in mind when establishing palliative care systems.*

CONCLUDING REMARK

Palliative care of patients with neurological disorder is a very young field, and virtually no data are available from the developing world. Therefore, this chapter can only constitute a first attempt at outlining some of the possible strategies in this field, and is lim ited by its being based on experience from a specific socio-geographical context (South-East Africa). We would therefore like to end by inviting criticism and contributions by all interested readers via email in order to improve the chapter in the next edition. Please address your comments and suggestions to Borasio@med.uni-muenchen.de – thank you!

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17 Subacute Sclerosing Panencephalitis (SSPE)

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INTRODUCTION

Subacute sclerosing panencephalitis / panencephalopathy (SSPE) is a devastating and largely preventable degenerative and ultimately fatal complication of measles infection.

The condition characteristically affects children and young people months to years after infection with measles(1). Prior to the introduction of the measles vaccination in countries of the developed world, the condition was rare - the annual incidence in the USA was 0.61 per 1,000,000 persons less than 20 years of age. The introduction of vaccination in the USA was followed by a 10 - fold reduction in incidence, and SSPE is now extremely rare. The situation unfortunately is very different for many countries of the developing world. Marked temporal and geographical clustering occurs. Papua New Guinea has the dubious distinction of reporting the highest recorded incidence. In a period of 46 months between 1988 and 1992 180 cases were diagnosed at the Institute of Medical Research in Goroka and in 1991 an incidence of 64.9 cases per million population less than 20 years of age was recorded – between 10-100 times higher than rates recorded from other countries(2). The high incidence has continued with 80 confirmed cases presenting to the Goroka base hospital in a similar period between 1997 and 2000 (3). Whilst SSPE is not an everyday presentation to the children's services Papua New Guinea pediatricians have all had experience in managing affected children.

The exact aetiology of SSPE is still incompletely understood. It is generally agreed that the incidence is inversely related to the age of infection with measles. Thus where there is a high incidence of measles in children less than 1 year of age there is likely to be a high incidence of SSPE in subsequent months and years. During the recent measles epidemic in PNG 75% of cases were less than 2 years and around 50% less than I year. In patients admitted to the county's only tertiary hospital, the median age was 11 months. Unfortunately this means that we can expect the high incidence of SSPE to continue for the next decade. Following the measles infection, which may vary in severity, the virus, which has by ill understood means gained access to the nervous system continues to escape immunological defense mechanisms and over a variable period of time produces progressive damage. Almost certainly both host immunological and viral characteristics are important in aetiology. DNA analysis techniques now allow identification of measles viral strains. A recent

study from PNG has shown that the viruses associated with SSPE are closely related to known strains, and are definitely not closely related to the vaccine strain(4).

SSPE is usually a condition of mid to late childhood, although it has been reported in children less than 1 year and in patients up to 30 years of age. In the Papua New Guinean reported series the mean age at presentation was 5.3 years in the first series and age of onset was 7.9 years in the second series(2,3). In an unpublished series of 19 patients from Port Moresby, the time from measles infection to diagnosis of SSPE was 4.4 years. Studies usually report a higher incidence in males than females although it should be realized that throughout the developing world there is an unequal male to female distribution of hospital admissions.

CLINICAL PRESENTATION OF SSPE

SSPE usually begins insidiously with mild and perhaps unrecognised changes in behaviour and in social interaction and (if at school) deteriorating academic performance. These "cerebral" changes progress at various rates to a state of dementia. Characteristic "motor" features are the onset of myoclonic jerks, which are generally symmetrical, and of hypertonicity. There are often other types of seizure and the hypertonicity may progress to a state of decerebrate rigidity and opisthotonus. Cerebellar ataxia and hypotonicity may sometimes occur. These progressive changes in cerebral and motor function lead to the child's inability to feed. In the absence of nutritional intervention, a state of severe malnutrition eventuates. This compounds the risk of development of bedsores resulting from immobility and incontinence.

At least 2 staging systems for SSPE have been proposed. The original system and the one most widely used was proposed by Jabour and coworkers in 1969(5) and has four stages:

Stage 1 Cerebral signs (mental and behavioral)
Stage 2 Convulsive motor signs
Stage 3 Mutism, loss of cerebral cortex functions, myoclonus
Stage 4 .Coma, opisthotonus

Staging the disease may assist the doctor in assessing its progress, but the stages overlap, and SSPE has a highly variable course. It may be rapid and inexorable, death occurring a few months after the earliest symptoms, or may be prolonged with periods of apparent remission.

DIAGNOSIS

Definitive diagnosis is confirmed by the finding of elevated measles antibodies in both serum and cerebrospinal fluid (CSF). This test is often not available and to a large extent diagnosis is based on the classical clinical presentation and progression. Experienced third world paediatricians will experience a sinking feeling at the presentation of a child between the ages of 4-12 with onset of "funny jerking movements" and deteriorating cerebral function. In the rare situation where EEG and CT scans are available, the former shows nonspecific abnormalities consistent with seizure activity and the latter is normal in the early stages, but shows progressive loss of brain substance

MANAGEMENT

Management of any long-term illness in children in a third world country is indirectly affected by the overall problems facing Child Health services. Populations are often mainly rural, whilst doctors are concentrated in urban areas. Even for those of the population living in the urban areas, access to health services is often severely limited. There are frequently problems with provision of safe water and sanitary faeces disposal. Malnutrition rates are high and children with a chronic disease such as SSPE may suffer other conditions, such as infected scabies and fungal infections. For many the germ theory of disease is a foreign concept. The prime concerns of curative disease services are the treatment of the common infectious illnesses, pneumonia, diarrhoeal diseases, malaria, meningitis, and tuberculosis. Facilities for the care and support of those with long-term illness are either absent or minimal. On the other hand there is usually a strong tradition of caring for family members, and it is accepted without question that mothers are admitted to hospital with their child, and undertake the daily caring duties that in a western context would be the domain of nursing staff. It is against this background that issues of management must be viewed.

Over the years a number of chemotherapeutic regimens have been applied to the management of children and young persons with SSPE. These have included inosiplex, interferon and cimetidine. Recent attempts have used combinations of inosiplex, antiviral agents and subcutaneous or intraventricular interferon alpha(6,7). None have been successful in curing the condition although some appear to have achieved temporary remission in progression or even temporary improvement. Given the varying natural history of SSPE however, it is difficult to be certain that temporary effects are definitely drug related. In any event the treatment regimens used are all very expensive and out of reach for the majority of children affected by SSPE. The components of management are therefore related to good nursing care and palliation and consist of the following:

CLINICAL ISSUES

Controlling Abnormal Movements

This is likely to be a frustrating task for the attendant physician and for the child and family. The typical myoclonic jerks are notoriously difficult to control, but in our experience a benzodiazepine is likely to be the best option. Clonazepam would probably be first choice but nitrazepam, which may well be more readily available and is likely to be cheaper, is an alternative (See Table 1, page 244). Controlling the other forms of seizure that are common manifestations of SSPE is likely to be equally difficult. Of the four broad-spectrum anticonvulsants, phenobarbital, phenytoin, carbamazepine and sodium valproate, the last is probably likely to be the best. Unfortunately its cost renders it unavailable to many patients in the developing world and in reality the choice of anticonvulsant is likely to be determined by availability. Whilst phenobarbital is no longer routinely used in a Western setting, it is a useful drug, is the cheapest of the anticonvulsants, can be given on a once daily basis and may be better than nothing. The side effects of impaired cognitive development and behavioral disorders that have limited its use in a Western context are not an issue in the context of SSPE, and in fact it is sometimes used in this situation in the developed world. Tablets can be crushed and administered via the nasogastric tube. Very few treatment centers in the developing world will have facilities for monitoring drug levels, but this should not deter the physician from using doses that might be considered high in other settings. The sedation that will accompany high doses may

well be helpful. Diazepam intravenously or rectally and paraldehyde IM or rectally can be used in an attempt to stop prolonged fitting (Table 1). Medical and nursing staff need to be aware of the respiratory depression that can occur when diazepam is used in a patient already on treatment with phenobarbitone. It is, unfortunately, our experience that the physician may have to accept less than optimal control of seizures.

Dealing With Muscle Rigidity

Muscle rigidity causing opisthotonus (arching of the back and hyperextension of the limbs) may develop during the course of the illness and is very distressing for the patient, caregivers and medical and nursing staff. It is very difficult to alleviate. It is highly unlikely that drugs such as baclofen will be available, and the only muscle relaxant that may be available, and is sometimes helpful, is diazepam. This is given orally (via nasogastric tube) (Table 1)

Table 1. Suggested Approaches to Clinical Problems

Clinical Problem		
Abnormal Movements/ Seizures	**Suggested Approach**	
1. Routine Prevention		
Myoclonic jerks	Nitrazepam ND	(0.125-0.5mg/kg oral 12 hourly)
	Clonazepam	(0.01-0.05mg/kg oral 12 hourly) Max 0.1-02 mg/kg per day
Other Seizures	Phenobarbitale	Loading 15-20mg/kg IM Stat Maintenance Daily 5mg/kg oral
	Phenytoin	Loading: 15-20mg/kg IV (1 hour) Maintenance: 2.5 5 mg mg/kg 12 hourly oral. Max. 250-300 mg per day
	Carbamazepine	Starting dose: 2mg/kg oral 12 hourly Max. 100 mg per dose. Increase to 5-1010-20 mg/kg daily
2. To stop the fit		
	Valproate	Starting Dose: 5mg/kg oral 8-12 hourly Increase to15-30mg/kg daily
	Diazepam	0.1-0.4mg/kg /dose IV, rectal
	Paraldehyde	0.1-0.15ml/kg/dose IM, may repeat in 2 hours 0.3ml/kg/dose* rectal * diluted 1:10
Muscle Rigidity	Baclofen ND	Starting Dose 0.2mg/kg oral 8 hourly Increase up to 1mg/kg oral 8 hourly tds
	Diazepam	0.05-0.1 mg/kg oral 4-6 hourly. Max. 5mg per dose.

Attending to Nutrition

Whilst some would feel that assisted nutrition has limited benefit in palliative care it is important to understand that SSPE has a highly variable course, which may extend over many months and even over several years. Many patients will be malnourished at the time of presentation to health services and malnutrition predisposes to the development of bed sores, making basic nursing care more difficult. In addition the use of assisted nutrition is important for the carers and family members, reducing their anxiety that their loved one will starve to death and increasing their involvement in patient care.

Table 2. Suggested Approaches to Clinical Problems

Nutrition		
	Water	1st 10kg 100ml/kg/day 2nd 10kg 50ml/kg/day subsequent Kg 25ml/kg/day
	Calories	1Kcal/ml of water
	Protein	1Gram/kg/day
	Vitamins	Folic Acid: 5mg weekly Multiple vitamin preparation Vitamin A 200,000 units stat if malnourished
	Minerals	Iron: 2mg/kg/day Trace mineral supplements* * if malnourished

The principles for SSPE patients are the same as those for other patients requiring assisted nutrition. In the earlier stages, the child will require assistance with oral feeding of normal foodstuff. As the disease progresses however, the ability to chew will be lost and it will be necessary to give liquid rather than solid food. Further in the course of the illness, pharyngeal coordination will be lost, and impaired swallowing will necessitate the use of tube feeding. Feeding tubes need to be firmly secured to avoid displacement, may block, and become hard over a couple of weeks- so that arrangements need be made for regular tube changing, ideally every 1-2 weeks. Where this is likely to be a major problem, the possibility of a feeding gastrostomy might be considered, though this is rarely performed for such an indication in the developing world, and, as is the case for tube feeding, carers need to be shown how to manage the device and to be comfortable in doing so before leaving hospital.

It is important to ensure that the daily requirements of water, and of micronutrients - electrolytes and minerals – as well as of macronutrients - calories and proteins - are met. One way of meeting most of these requirements when solid food is no longer practicable or possible and when tube feeding is required is with milk fortified with vegetable oil and sugar. Vitamins and a basic mineral solution (containing zinc at least and potassium and other trace minerals at best) if available should be added to the milk oil mixture.

Table 2 shows the daily requeriments values used for calculation of the adecuate requeriments. For example a child of 25 Kg requires 1625mls of water and approximately 1625 kcals daily, and 20-30gm protein. 1625 ml of unmodified cows milk formula (67kcal/100ml) contains inadequate calories for daily requirements. The same amount of milk oil formula (10ml vegetable oil and 2 heaped teaspoons of sugar per 200mls milk) will provide adequate calories as well as adequate amounts of digestible protein. The total daily amount should be given as 6 to 8 feeds spaced throughout the 24 hours. Ideally daily iron requirements (2mg elemental iron/kg) should be provided in the form of iron suspension or crushed ferrous sulphate tablets. Folic acid tablets should be given on a weekly basis. Alternatives to milk include cereal gruels or soups made from locally available vegetables and other food sources. In rare instances families may have access to and can afford more expensive commercially prepared forms of liquid nutrition.

There may come a point in the deteriorating natural history of the disease at which some physicians might feel that further nutrition support is unwarranted, prolonging suffering for the child and the family, and delaying the inevitable. It would, however, be highly unlikely that the patient's family members would agree with this view. They would likely be highly surprised that the necessity of continuing feeding would be questioned - even though it may be a burden for the family. Whilst accepting that the patient will die they would almost always regard feeding as their responsibility towards the patient, and see withdrawal of feeding as abandonment. Medical and nursing staff may, during their prior discussions with the family, suggest that a time might be reached when the child is suffering too much, and when withdrawing feeding, and hastening the end of the suffering, may be the kindest thing to do. Medical and nursing staff, should, however, always respect the family's decision.

Prevention of Bed Sores

The reality for most patients with SSPE in the developing world is that they will be hospitalized in institutions with nurse: patient ratios that would be considered to be unacceptably low in a Western context. Table 3 shows the basic nursing procedures such as regular turning, washing and bed making. Care of early bedsores to prevent progression, which are taken for granted in the latter, are often inadequately performed. These duties almost inevitably fall to the guardians. It is imperative, therefore, that the guardians are correctly instructed in the correct techniques and as far as is possible are given regular support and encouragement. Patients should be turned regularly (one to two hourly as far as is practical), and soiled or wet bed linen should be changed as soon as possible. The patient should be washed daily and as required. The first sign of a bed sore may be reddening of the skin over pressure points such as the hips, the iliac spine, the sacrum, heels and elbows. Caregivers should be shown how to check these areas, and gentle application of emollients such as zinc cream, Vaseline, coconut oil or other locally available preparation may be helpful in preventing progression. Bed sores that have already developed should be cleaned with previously boiled water, if possible containing a little salt (a finger pinch of salt to a cup of water, or a level teaspoon to one litre), and covered with dressings, using Vaseline or zinc cream to prevent sticking to the sore if possible. Large bedsores with slough (dead tissue) can be treated by the application of regular saline dressings. Application of papaya (pawpaw) may also be effective. Some form of padding such as pillows or home made cushions should be used to minimize pressure on the affected part of the body.

Table 3. Suggested Approaches to Clinical Problems		
Bed Sores		Turning - ideally every 1-2 hours Preventing contact with soiled or wet bedding Regular washing to keep skin clean Examination of pressure areas for early signs Gentle application of emollients eg coconut oil Cleaning and dressing early sores Saline soaks to soften and remove slough Use of padding, cushioning, to alleviate pressure
Incontinence		Condom Drains, manufactured or devised Suprapubic stimulation of voiding reflex Catheterization
Constipation		Regular palpation of abdomen Early use of oral laxatives (eg coloxyl, sennakot) Suppositories, enemas if necessary
Fever		Consider and treat infections as appropriate
	Paracetamol	Oral 10-15 mg/kg 6 hourly Rectal 30 mg/kg 6 hourly Tepid sponging.

Dealing with Incontinence

Incontinence is an inevitable feature of SSPE as voluntary control is lost. The management of incontinence is difficult but important. Absorbent nappies are a luxury that most patients and most health institutions in the developing world cannot afford. Manufactured uridom drainage systems for male patients are sometimes available, but more often it will be necessary to use a condom, spare tubing or drainage bags and ingenuity to prepare a home made device. Guardians can be taught to induce urination by gentle repetitive pressure over the suprapubic region to stimulate the voiding reflex, catching the urine in a bedpan or other container. It is worth persisting with this approach, which can become a routine part of care, with regular voiding 2-4 times daily. If these techniques are unsuccessful, it will be necessary to catheterize. Although intermittent catheterization might be possible in some circumstances, "permanent" catheterization is likely to be the easiest and the preferred option. Parents and guardians should be given instruction in the care of the catheter and the need for monitoring urinary output and feeling for bladder distension, so that they are comfortable with this aspect of management when they decide to take the child home. Arrangements will need to be made for changing the catheter when necessary.

Preventing Constipation

The low fiber diet that is of necessity given by tube feeding or gastrostomy, together with the child's bedridden status will inevitably lead to constipation. It is important to discuss the frequency of bowel motions with the carers and to palpate the child's abdomen for a build up of faeces in the colon. Simple oral laxatives such as senokot or coloxyl should be used freely, and laxative suppositories when necessary. Faecal impaction should not be allowed to occur, but should it do so, enemas will be required.

Dealing with Fever

Fever may be due to an infective process or to damage to the hypothalamic temperature-regulating centre. Malaria, respiratory viral infections, urinary tract infections and pneumonia should be considered. Routine and locally appropriate antimalarials should be available to treat malaria. Chronic urinary tract infection is almost inevitable with prolonged catheterization and a low-grade temperature from this source may be acceptable. High fevers should in most cases be regarded as an indication for examining and if possible culturing the urine. Urinary antibiotics such as cotrimoxazole can be given orally or by nasogastric tube and for those with a catheter, this should be changed. Antibiotics may be used to treat pneumonia. Decisions on the use of life prolonging treatment such as antibiotics for pneumonia are difficult. They should be made in consultation with the patient's family, and will depend, among other considerations, on the stage of the SSPE.

Paracetamol is the mainstay of therapeutic management of fever. It can be given orally or via nasogastric tube (as crushed tablets or syrup). Whilst not as effective as paracetamol, tepid sponging is certainly beneficial and is likely to be more readily available.

Terminal Care

There are some similarities and some differences in attitudes and expectancies surrounding death between peoples of different cultural and religious backgrounds. A recent study in adults has shown marked differences in felt needs between those in a developed and those in a developing world context(8). Those in the former indicated that material needs were generally well catered for, but that support from family, friends and community was often lacking. In the latter, the reverse was true, the needs being material (such as adequate pain relief and medical supplies), whilst support from family and friends was usually provided. In developed countries there may be palliative care teams, particularly nurses, but often also doctors, volunteers, social workers, physiotherapists and pastors or chaplains who may visit the family at home. They are able to give moral support and nursing care, bring nursing or pharmaceutical supplies and provide respite for the carers. Occasionally there may be a crisis when the patient is readmitted to hospital or, when one is available, a children's hospice. In the developing world such home services are unlikely to be available, and the family carers will make do as best they can, perhaps with intermittent assistance from a local health clinic

In both developed and developing worlds, patients with terminal conditions are likely to wish, if possible, to be cared for, and to die, in their familiar home surroundings and among family and friends. These attitudes are likely to apply to those caring for a dying child. It is common practice in the developing world for guardians to indicate that they wish to take their child home. Doctors and Health staff should be prepared to accept and respect this decision and to ensure that as far as possible the material needs for managing the patients (eg medications, urine draining devices) are provided or available.

EMOTIONAL SUPPORT

An Honest and Supportive Approach to the Child, Parents and Family

It is essential that medical and nursing staff build an honest and supportive relationship with parents and family. The mother and other main carers may themselves require minor or even major medical

attention during protracted care giving, and hospital staff should ensure that this is provided easily and promptly. This may include ensuring easy access to antenatal or family planning services, or simply providing analgesics for a headache or backache.

In relation to the disease itself, the hospital staff should, as soon as the diagnosis is suspected, explain that their child has a serious condition for which there is no curative treatment. Even if definitive laboratory diagnosis is available, the results may take some time to arrive and parents and families should not be kept in suspense. Explaining the nature of the condition and its progressive course is likely to be a painstaking task. The extent to which the medical staff divulges the details of the course of the disease will depend on how much the family wishes to know at a particular time. It may take time for the information given to sink in, and information may require repetition. It may well be helpful to discuss aspects of previous experience of caring for patients with SSPE. This indicates to the parents that they are not alone- other families have been through the same experience. It also indicates that the medical staff has had experience of caring for patients similar to their child. Questions from the family must be answered both honestly and sympathetically. It is important that the family understand from the start that there is no cure for SSPE and that the medication provided is to try and control the symptoms of the disease, such as myoclonic jerking and other forms of seizure, and to maintain, as far as possible, the child's general health and nutrition. Sometimes families will go to desperate lengths to help their child. They may plan to transfer to a bigger health facility for a further opinion and where more investigative facilities are available. They may raise the possibility of going to an adjacent or overseas country. It is important that the medical staff listens to these requests, and is frank about what can be expected from such transfers. The trauma, emotional, family and financial that can arise from ill advised transfers should be stressed, and it should be pointed out that the kindest and best way they can help their child is to care for him or her in their local surroundings, with the available family support. Should the family decide to transfer, however, the medical staff should ensure them of their good wishes and of their willingness to continue care on their return. On the other hand, should the family wish to be transferred to the care of a health facility nearer their home, the medical staff should facilitate this and make sure appropriate information concerning the child's management is provided for the local health staff. Many such health facilities, whilst not staffed by a pediatrician may well have trained and motivated nursing and ancillary staff who are equally capable of providing the required care.

An Understanding of the Family's Cultural Background and Spiritual Needs

Many families in developing countries will, as previously mentioned, have their own beliefs about health and about disease causation. These may include the belief that illness is the result of family conflict, "payback" and sorcery. It is important that the doctor caring for the child appreciates and respects these beliefs. Parents may sometimes request that they be allowed to take the child to see a traditional healer, or that they be allowed to bring a traditional healer to see their child. The doctor must appreciate that they are doing what they think is best for their child (as would the doctor in similar circumstances) and should be supportive as far as is practicable.

Most families will have a religious affiliation, and many will have deeply held religious beliefs. Irrespective of the doctor's own personal affiliation or belief, the families should be encouraged to

seek the support of their pastor, priest, mullah, or other appropriate spiritual counselor. The rights of those from minority religions or sects are as fundamental as those from the majority. Spiritual support will help the family to come to terms with the situation, to remove feelings of guilt or blame, and to help with the healing process that is necessary for care takers. It is most important that the parents come to be at peace with themselves- knowing they have done all that they can for their child

Treating the Patient as a Person

It is all too easy to forget that the patient who has been in the ward for some time, who cannot communicate and who is being treated with large doses of anticonvulsants is a person. Taking time to examine the patient, to talk to him or her, and perhaps to hold his or her hand whilst talking to the family, will help the doctor to remember this paramount fact. It will also help in assuring the parents and family that medical and nursing staff is still interested in their child and still caring. Scabies and skin sores and minor medical problems should be dealt with promptly and carefully.

CONCLUSION

The prevention of measles and thus of the overwhelming majority of cases of SSPE is in theory very straightforward. Measles vaccination virtually eliminates SSPE. In reality, providing the very high coverage of measles vaccine (95%) that is required to prevent measles outbreaks is extremely difficult in many countries of the developing world(9). Whilst there has been considerable improvement in immunization coverage in many countries over the last decade, there are many, including PNG (currently at less than 50% coverage) in which rates are far below the required level. In efforts to achieve high coverage some countries, notably in South America, have successfully adopted Supplementary Immunization Activities (formally termed National Immunization Days) to supplement the routine vaccination schedules of infancy. Predictably, the countries with the highest incidence of SSPE are likely to be those with the greatest difficulties – geographic, financial, and social – in delivering measles vaccine to their children. This is – or should be- a matter of international concern.

Unfortunately, SSPE is likely to continue to occur in resource poor countries. It is certainly not the only condition for which palliative care is required. Others include untreatable and terminal cancers, renal failure, and other neurodegenerative processes. It is therefore important that the issue of palliative care in resource poor countries is given close attention and that provision be made for appropriate and effective care both in hospitals and communities

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18 Home Care Issues

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During the past century many changes have occured in the medical practice. One such change is the location where patients die — it is no longer at home, but in an institution. Approximately one third of all terminal patients die in their homes. This happens in spite of reports which indicate that between 50 and 80% of seriously ill patients prefer to stay at home during the final days of life — and die there if possible.

PALLIATIVE HOME CARE

The main goal of palliative care is to provide the necessary resources to insure the best possible quality of life for the patient and family as they face an incurable illness. With this goal in mind, patients should be provided the opportunity to die in their homes if that is their wish.

The palliative care team should provide the best care in the home for as long as possible. Most patients with incurable advanced illnesses do not have the choice of receiving Palliative Home Care and therefore die in institutions. Reports from developed countries show that when patients receive adequate palliative home care, the number of deaths at home increases. A USA study (1995) reported that 74% of patients who received palliative hme care died at home.

The information available from developing countries on the number of patients who receive palliative home care and die at home is scarce, but it is estimated to be very low with the majority of patients dying in institutions. In Argentina, there is no information on the percentage of patients who receive palliative care, but it is estimated to be below 5 %. The percent of cancer patients who receive palliative care through the Programa Argentino de Medicina Paliativa-Fundación FEMEBA (PAMP) and die at home varies with the program — 50-85 % in the Centro de Cuidados Paliativos (CCP) San Nicolas, 60 % in the Unidad de Cuidados Paliativos (UCP) Sommer and 17 % in the Unidad de Cuidados Paliativos (UCP) Tornú.

This chapter describes the main issues related to palliative home care, the barriers in the provision of such care, and the experiences of three different programs in Argentina; CCP San Nicolás, UCP Sommer and UCP Tornú.

ETHICAL ASPECTS OF PALLIATIVE HOME CARE

PHC aims to redefine the approach to care of the patients with advanced disease. The choices of where assistance is received at the end of the life, and the place of death, are important concerns of patients and families. The options should be evaluated using accurate and complete information of the cost/benefit ratio, and the patient, family and team should agree upon them. The possibility to change an approach must be assured.(*)

The PHC team should be careful not to intrude in the privacy of the home or disturb family life. In order to avoid those inconveniences, a balanced activity should be planned that considers the needs, the cost/benefit ratio of intervention and the operational and organizational skills of the family.

The PHC must not "over-medicalize" or "technify" the dying process. Palliative care is a medical discipline that utilizes all available diagnostic and therapeutic practices, even those of high technology. But the selection of which approach to use, and when to use it, should be based on a cost/benefit analysis of each unique situation. With this analysis, life prolonging devices and measures (i.e. mechanical ventilation, vital monitoring, dialysis, parenteral nutrition) should not be offered or included in PHC plans. They do not comply with the proportionality principle and favor "hospitalization at home" and over-"medicalize" the dying process.

The election of the place where care is given should be made without the influence of economic factors. The goal of PHC is not to reduce costs, but to improve the quality of life. It is probable that there can be savings for the healthcare system, but it should not be forgotten that there are economic burdens on the family. If PHC is promoted and implemented, resources must be provided — the minimum is to provide medication (i.e. opioids), and the maximum is to assign funds to the caregivers who are in charge of the assistance.

PALLIATIVE HOME CARE DEVELOPMENT

Appropriate and ideal care during the final phase of life requires:

(a) An interdisciplinary team to evaluate and treat the social, psychological, physical and spiritual needs of patients and their families, and;

(b) Flexibility so care activities are adapted to the changing needs of the patients including outpatient care, home care, day care or hospital care. Complete interdisciplinary teams are rare and partial palliative care is the most common model of care in the final period of life— especially in developing countries. In Argentina, the development of palliative care programs occur when a group of volunteers (physicians, trained non-professional individuals, nurses, psychologists), who work in an institution or in the community, begin an outpatient activity without equipment or infrastructure. As more resources become available, they then progress towards a complete service. Table 1 shows the developmental stages observed in several palliative care teams in Argentina.

Table 1. Development stages of a PC team					
STAGE	**1**	**2**	**3**	**4**	**5**
CARE	Outpatient ☎ Home Care	Outpatient ☎ Home Care	Outpatient ☎ Home Care Designated beds	Outpatient ☎ Home Care Designated beds Day Care	Outpatient ☎ Home Care Designated beds Day Care Palliative Care Unit
TEAM	Physician Volunteers Nurse Psychologist Basic training Part time				Inter-disciplinary basic & complete training part & full time
Few Teams reach stage 5					

☎ Follow up by phone/call-in options

The home care components of programs vary in complexity and effectiveness. During the first stage of development, the patient is cared for primarily by a responsible caregiver and the team's activities occur mostly in the office where contact with the patient tends to be by phone rather than through home visits. In the subsequent stages of development, care continues to be the responsibility if the caregiver, but home visits and assistance are added as the team's capacity to carry them out (personnel, time, transportation, etc.) increases. The stages are not static – activity is modified continuously as the team develops and changes its characteristics. The team characteristics which may influence the outcome of home care are: degree of institutional support, availability of resources for delivery of home care (vehicles and drivers), whether care is provided free or for a fee, the number of disciplines involved in the care, the time dedicated to providing care and the adequacy of staff training. Different combinations of these characteristics determine the complexity and financial outcome of the care provided.

Examples:

1. *A stage one team is developed in the community where there is institutional support and offers care to outpatients. When patients are unable to visit the institution (due to long distances, poor clinical condition, or lack of transportation), "distance" palliative care home is instituted using the following steps: (a) the caregiver provides clinical information about the patient by phone, (b) a presumptive diagnosis is made, (c) the caregiver receives verbal and written instructions about specific treatments and continues to care for the patient at home and (d) when the patient gets worse, he/she is hospitalized.*

2. *A stage two team is developed in the community with institutional support to offer care to outpatients and to make home visits. When the team is not available (nights, week-ends) the institution's physicians participate in the care and the caregiver is provided a summary of the clinical record, the medications to use and therapeutic suggestions in case of a crisis.*
3. *The level of impact of a care program on the place of death is directly related to whether the team is able to offer home care: The UCP Sommer team (stage 5), located in a rural area, has vehicles, drivers and travels 7,000-10,000 Km per month making home visits: 60% of their patients die at home. The UCP Tornú (stage 5) in Buenos Aires does not have vehicles or drivers and only a few home visits are made to patients who live very close by: 17% of the patients die at home.*
4. *Free Care vs. Fee for Service: The CCP San Nicolas (Argentina) offers palliative care while charging only a small fee to patients with health coverage. Under this model, the team (2 physicians, 2 psychologists and 2 nurses) is always available and their assistance is delivered at home: 85% of their patients die at home. Some members of the team also offer free consultations in the office each week, to very poor patients. However, when the patient deteriorates and is unable to travel to the office, he/she usually ends up being hospitalized: 50% of these patients die in an institution, cared for by other professionals.*

These results seem to indicate that if the patient needs to be hospitalized, the number of hospitalization days and the percentage of deaths in the institution, decrease when the quality and access to home palliative care increases. These values can be used as indirect indicators of the efficacy of the programs.

ADVANTAGES OF PALLIATIVE HOME CARE

1. *The patient has more autonomy. He/she remains within the family and maintains some decision-making power over his/her own activities, rest and diet, without the strict regulations imposed by institutions. In addition, the patient can perform some tasks at home and maintain, to some degree, his or her lifestyle.*
2. *The patient has more privacy. He or she is not exposed to interferences by unnecessary, and undesired, medical procedures. Also, the patient is not exposed to the suffering of other patients which allows them to be calmer at home. Institutions are not prepared to provide care and assistance at the end of the life— this may create feelings of abandonment and loneliness.*
3. *The patients in home care are "protected." At home they are less exposed to useless and unnecessary therapeutic procedures during the advanced stages of their disease (ICU, parenteral nutrition, etc.)*
4. *Since the family is continuously involved in the care of the patient at home, they are better prepared for the bereavement process as compared to patients treated in the hospital. The discomfort surrounding a death at home can also be reduced if the last days are spent where life was shared. The process may be less terrifying, distant and aberrant —the lesson learned is that death is a stage of life.*
5. *The quality of symptom management and the cost of assistance vary. If the care is efficient and effective, it can be similar to that offered by an institution with a palliative care unit; but it certainly can be better than the care offered by an institution without one. The cost of care delivered in the home may be lower for the healthcare system if futile care (over utilization of medication and technology) is avoided.*

DISADVANTAGES OF PALLIATIVE HOME CARE

In some cases, home palliative care may result in increased anxiety and the possibility of a family crisis. Although, by staying at home, the patient may partially return the equilibrium to the family, this equilibrium may be disturbed by the disease progression and by the changes in the patient's mood and behavior. The family members, who witness the patient's progressive deterioration, suffer and may experience various emotions (fear, frustration, guilt, anger) which can cause mental health disorders. In addition, the disease may have a negative impact on the family's economic and financial condition due to expenses associated with the medical treatment, the fees for the healthcare personnel and the reduced income associated with work absenteeism.

Situations in which Home Care is not Appropriate

In some situations home palliative care is difficult or impossible to provide. Some of the reasons are:

a. The patient wishes to be hospitalized

b. Patient does not have a family or the relation with his/her family is broken and deteriorated (Primary reason for hospitalization of patients in the UCP Sommer Program)

c. The home is uncomfortable or lacks the necessary facilities (bath, kitchen) (Primary reason for hospitalization in the UCP Tornú Program)

d. The family is physically tired or emotionally weak

e. Uncontrolled symptoms or situations capable of generating severer anxiety or discomfort (convulsions, hemorrhages, odiferous tumors, fecal incontinence)

f. Frequent need of medical or nursing procedures

SPECIFIC ASPECTS OF PHC

Responsible Caregiver (RC)

The availability of a team and other resources does not guarantee appropriate palliative home care. The cornerstone of care is the family, and at times, it may be incapable or unwilling to provide the necessary care to the patient. Members of the family must be integrated into the team because they are the informal full-time caregivers who work without fees, and do so based on pre-existing relations and altruism. If the integration of the family into the care process is achieved, the majority of the patients can remain in their homes until death.

Study

In the CCP San Nicolas, the caregivers for 50 consecutive patients were interviewed about aspects of the care process including:

- *their degree of suffering and its causes (Suffering Scale, Memorial Sloan Kettering Cancer Institute (MSKCC), National Cancer Institute (NCI)1.0);*
- *the emotional and practical difficulty of care tasks (0-10 scale: 0 without difficulty, 10 maximum difficulty);*
- *their satisfaction with the caring tasks (0-10 scale: 0 dissatisfied; 10 maximum satisfaction);*
- *the sufficiency of family incomes during the period of home care (0-10 scale: 0 not enough for anything, 10 permits savings); and*
- *the negative economic repercussions of providing home care (0-10 scale: 0 none, 10 maximum).*

The results of this study are described further in this chapter.

Integrating the Family

1. *Evaluate whether the family is practical and emotionally able to assist the patient*
   - *Do they wish to do it?*
   - *Is their socioeconomic condition and health coverage enough to cover the costs of the treatment?*
   - *Will they be able to continue with their jobs?*
   - *Do they have the capacity to understand and comply with the treatments?*
2. *Identify the responsible caregiver.*

   The caregiver is the member of the family who is in the best condition (health, relation, proximity and availability of time) to carry out and coordinate the care. Usually this person is a relative; but at times is may be a neighbor, a friend or a member of a religious community. In the study group described before, 81% were women, 54% children and 32% spouses or couples. The average age of the caregiver was 46 ± 15 years. In all cases, the same relative provided care during all treatment periods.
3. *Train the caregiver.*

   It is necessary to progressively train the caregiver in care and comfort techniques with simple verbal and written instructions so that he/she can carry out these tasks appropriately. (*)

Areas of Training

- *Administration of medications (i.e. How to comply with dosage schedules, to measure syrups, to place suppositories, to do SC injections, etc)*
- *Monitoring and recognizing different aspects of symptoms: vomiting, pain, dyspnea, cough, insomnia, constipation and delirium. They must be able to identify and record the duration and frequency of these symptoms as they occur during the day.*
- *Diet and hydration*
- *Control of depositions*
- *Hygiene (bath, oral cavity)*
- *Changes of position, dressings*
- *Organization of the family tasks*
- *Recognition of the stages of the death process.*

  As the intermediary between the team and the family the caregiver must be knowledgeable about the patient's clinical condition, and also be able to provide the necessary information about his/her care.

In the study group, the caregivers at the end of the treatment reported a low score (2.32 ± 3.5) in difficulty in carrying out the tasks as well as a high score (8.9 ± 1,6) in satisfaction of having performed them.

4. *Support the RC*

   Lack of support for the caregiver is a frequent cause of hospitalization of the patient. The task and the responsibilities of the caregiver are full-time and can be stressful— the illness, the home care and the tasks can generate many doubts, some of which are:

Medication concerns

- *Drugs and doses: when to increase the dose and fear of overdosing.*
- *Undesirable effects*
- *Treatment and interventions*
- *Potentially hazardous effects*

Choice of the appropriate therapeutic options
What do symptoms imply or mean?
Operating dichotomies

Prioritize the personal needs of the caregiver vs. those of the patient
Since doubts and uncertainties will always exist, caregiver support can be provided by:

1. *An effort to maximize symptom control, the availability of a palliative care team and the support of a healthcare institution.*
2. *A care plan and a schedule of activities.*
3. *A knowledge base that anticipates the changes that may occur in the patient's condition, and information on how they will be corrected, such as:*
   - *Undesirable effects of the medication and of the illness.*
   - *Feeding difficulties.*
   - *Progressive weakness and the gradual increase of dependence.*
   - *Sleeping disorders and delirium.*
   - *Mood changes.*
4. *Measures used to reduce the emotional load of the RC.*
   Teams in stages 1 and 2, such as in the CCP in San Nicolas, invite caregivers to participate in psycho-educational meetings of 1-2 hours duration every 2-4 weeks. During these meetings, which are coordinated by a psychologist, the RCs are allowed to reflect on their own experiences, voice their fears and concerns and learn from each other. Doubts are analyzed and the provision of resources is optimized. In more developed teams, the RC is assisted during office visits or hospitalizations.

   In the study group, caregivers reported moderate emotional difficulty (5.7 ± 3.8) in providing home care. They also reported high suffering during the course of treatment, with no difference between the initial (7.5 ± 2.8) and final (8.4 ± 1.8) evaluations after a mean duration of 39 (± 11) days. The main reported causes of suffering were their own emotional situation, the emotional and physical condition of the patient, and economic problems.
5. *The Need for Material resources.*
   When promoting PHC the necessary resources must be assigned to the patient and caregivers: medications, beds, wheel chairs, funds to compensate for the family's increases in expenses and their reduced income. In palliative home care, someone must stay with the patient, the family is responsible for buying supplies and medications which in Argentina are otherwise provided free of charge in the hospital. Generally, there is an under-reporting by caregivers of the negative impact and damage caused by the situation, in spite of experiencing a deteriorated economic situation and limited financial aid. In the study group the caregiver reported a score of (2.2 ± 1.9)

for the sufficiency of family incomes during treatment, and (1.8 ± 2.8) for the negative economic repercussion of home care. Although the family's capacity of adaptation to these adverse situations seems unlimited, it is a fact that providing home care generates an important economic deterioration.

SYMPTOM CONTROL

Symptom control is carried out according to the criteria established by WHO. It is important:

- *To guarantee the provision of drugs, especially opioid analgesics. In developing countries the high cost of commercial opioid preparations is a barrier to adequate pain treatment. One option that guarantees the provision of these drugs free of charge, or at a low cost, is to use preparations compounded by a local pharmacist— for oral use, aqueous solutions of morphine (6 mg. /cc), oxycodone (3 mg. /cc) or methadone (1 mg. /cc). For subcutaneous use, aqueous solutions of morphine or oxycodone (10 mg. /cc) are sterilized in cold and passed through micropore filters. Compounded preparations for oral use such as dexamethasone, metoclopramide, hyoscine, bisacodyl, haloperidol, paracetamol, etc. are also useful.*

- *To monitor the treatment. In PHC where patients may stay variable periods of time without medical evaluation (stages of development 1, 2 and 3), it is necessary to update information about the patient's clinical condition in order to make the necessary changes of the treatment plan. A semi-structured symptom evaluation tool enables team members (volunteer, nurse) to uniformly monitor treatment on a regular basis. The information is obtained from:*
  1. *The patient, when he or she comes to the office or during a home visit. The PAMP uses a form to collect the date and location of consultations, clinical disorders, symptoms [Edmonton Symptom Assessment Scale (ESAS)], cognitive disorders, level of hydration, frequency of bowel movements, hospitalizations, route and doses of opioids, use of adjuvant drugs, and diagnostic and therapeutic practices (*).*
  2. *The RC, when he/she comes to the office or through telephone calls. The RC reports the patient's condition using a form that lists 22 symptoms—11 of which have yes/no options while the remainder obtain information about the intensity and frequency using two Lickert 4 scales (*).*
- *To avoid "hospitalization at home," the type of the interventions that are carried out during the PHC should be regulated. The following interventions/procedures can be performed at home: different routes of administration for medications, psychological interventions, lab tests, thoracic/peritoneal drainage, dressings, rectal maneuvers, physical therapy, ECG, chest/abdominal X-ray, hypodermoclysis, blood transfusions, bladder catheterization, oxygen supplement, etc.*

At the CCP San Nicolás the 3 most frequent procedures are SC infusion of drugs, enemas and hypodermoclysis; the 3 most frequent diagnostic practices are plain X-rays, ultrasounds and electrocardiograms (ECG), and the 6 most frequent lab tests are CBC, creatinine, electrolytes, blood sugar, calcium and PT and PTT.

- *To carry out the psychological evaluation and assistance to the patient. Since psychological assessment is not always possible for all patients, it may be performed when:*

1. *The patient comes to office or during hospitalization.*
2. *There is an established set of criteria that specifies when a patient, or a team member, may request evaluation because of a risky situation—where there is lack of treatment compliance, anguish, sadness or insomnia that is rated 6, or more, on the numerical scale of 0 to10.*
3. *There is a semi-structured evaluation based on the DSM4 axes system.*
4. *After brief psychotherapeutic practices: analysis of problems, behavioral techniques, cognitive techniques, and relaxation techniques.*

FINANCIAL ASPECTS

The direct cost of PHC is related to the intensity of the assistance, the number of professionals that intervene, and the use of therapeutic and diagnostic resources.

Assistance cost. The items that generate costs are:

1. *Number of visits by each professional (with the specific practices of each discipline)*
2. *Type of drugs and dosages*
3. *Medical supplies*
4. *Diagnostic and therapeutic procedures*
5. *Medical equipment (i.e. wheel-wheels, pneumatic mattresses, etc) needed*
6. *Operational expenses (i.e. vehicle, communication, distance to the home, secretary, office setup, etc)*

If each team determines the average utilization for each item and knows their value, it is simple to structure the assistance cost over a period of time.

The CCP San Nicolas charges the HPC by using modules of assistance that have the same cost for all patients. The items that are included in the cost of one month of assistance are:

1. *Medical and Nursing visits: One per week at the beginning, with patients in stable clinical condition and controlled symptoms; One or more per day in the final period; each visit in the coverage area demands an average of 2 hours.*
2. *Four psychology/counseling interviews with per month -two per month for the patient and 2 for the family*
3. *The provision of oral and parenteral opioids analgesics — the average daily oral dose of methadone is 30 mg (with 3 - 30 mg oral morphine rescue doses), or an equivalent parenteral dose of an analgesic is provided.*
4. *Regular, and on-call, medical and nurse home visits within a 20 km radius, but excluding hospitalization.*
5. *It also includes oxygen, life support measures, palliative RT and QT, diagnostic practices, lab tests and medical supplies and equipment.*

Use of healthcare resources. The utilization of resources was evaluated in CCP LALCEC San Nicolas (stage 2, an exclusive home care program) and in UCP Tornú (during it's stage 4, assistance in office and hospital). The patients had free access to all resources and both teams had similar training and therapeutic approaches. The utilization of therapeutic and diagnostic resources by cancer inpatients, with similar clinical conditions, was compared (see Table 2).

Table 2. Use of resources in PHC and during hospitalization		
VARIABLE.	**CCP LALCEC 1996**	**UCP Tornú 1999**
# of patients	48	50
ECOG*in the first consultation:	26 good 22 bad	24 good 26 bad
Length of treatments (days, m ± SD)	70.4 ± 62.3	80 ± 61
% of hospitalized patients during treatments	21 %	100 %
Days of hospitalization (m ± SD)	1.1 ± 2.3	13 ± 9.9
% of home deaths	85 %	17 %
# of consultations (m ± SD) to extra-team professionals	0.6 ± 0.6	0.6 ± 1.2
# of diagnostic practices (m ± SD)	2.1 ± 1.9	2.9 ± 2.0
# of therapeutic practices (m ± SD)	3.0 ± 1.2	2.6 ± 1.6
# of lab tests (m ± SD)	8.6 ± 4.5	7.9 ± 7.6

* Eastern Oncology Cooperative Group- Functional Capacity Scale (0-4) GOOD (1+2) / BAD (3+4)
m – median

There were significant differences between the two centers with respect to the % of patients hospitalized, the length of stay of the hospitalization and the % of deaths that occur at home.

It has not been verified that PC results in a savings by reducing the expense of fragmented care or the use of high-tech interventions. The studies are not final because of methodological problems— some do not show savings, while others show saving of up to 68 %. The PHC should be able to produce savings by reducing the number and the length of the hospitalizations.

In our experience, PHC under the direction of an experienced team that does not carry out unnecessary diagnostic or therapeutic interventions, and incorporate the family as part of the care team requires resources similar to institutional care. It can generate savings by reducing the number and length of the hospitalizations.

VOLUNTEER'S ROLE

The participation of volunteers from different professions and social groups in a healthcare team increases labor resource and improves interaction within the community. If volunteers receive adequate training, they can greatly increase assistance to patients and family at all developmental stages, especially in stages 1 and 2.

Some of the volunteer tasks that can impact:

- *Semi-structured evaluation of the patient, at home or by phone.*
- *Performing massages, helping with diet and hygiene.*
- *Practical support (to prepare the food, hygiene of the home, transfers, purchases).*
- *Recreation (companionship, walks).*

BARRIERS TO THE DEVELOPMENT OF PALLIATIVE HOME CARE

The multiple system and resource barriers to the implementation of both PC and PHC can be grouped as follows:

The Healthcare System

1. *PC is not included in health plans. There isn't a budget assigned to PC and there are no reimbursements for PC expenses.*
2. *Few public, or private, health plans offer PC and few plans recognize the need for home care for chronic diseases.*
3. *Generally, when provided, PHC lacks good quality— home visits are not carried out with the necessary frequency, and patients do not receive adequate symptom control. The communication between professionals, patients and families is faulty, and fragmented, and the multidisciplinary team does not analyze all treatment options.*
4. *Institutions guarantee to patients the availability of physicians, symptom control, medication (i.e. strong opioids) and other resources, but in most cases, such guarantees are not available in PHC.*
5. *Families, the key component of home care, do not receive adequate support or training. Family members are usually tired, have emotional crises and suffer economic deterioration.*

Healthcare Professionals

1. *Do not act as part of a team to offer integral care*
2. *Do not have experience in home care*
3. *Do not have training in communication, and do not inform the patients correctly about care options*
4. *Do not know PC philosophy and do not use the available knowledge for symptom control*
5. *Do not integrate the family into the care process; are unaware of the need, do not put value on the link between patient care and the impact that the disease has on the family's daily activities 6.*
7. *Cannot charge fees for providing PC at home.*

Due to these barriers, the institutional care model is still widely accepted in the community. In order to reduce or eliminate these barriers, healthcare policies need to be adopted to make home care a component of a system that offers assistance and education.

CONCLUSION

Palliative home care is not a high technology approach to care at the end of life, but a type of care delivered by a multidisciplinary team dedicated to improving the quality of life of both the patient and the family. At times the special problems that prevail in the patients' homes, not only make it a challenge, but also a source of satisfaction. When good quality PHC is provided, the patient receives the best possible care.

Suggested Readings:

Facing death: new themes in palliative care. Eds: Clark, D., Hockey F. and Ahmedzai, S. Philadelphia: Open University Press, 1997. ISBN 0-335-19605-5

The future for palliative care: issues of policy and practice. Clark, D. Philadelphia: Open University Press, 1996.

Oxford Textbook of Palliative Medicine. D. Doyle, G.W.C. Hanks and N.MacDonald Oxford University Press, 1997 ISBN 0-19 262028 2 (Hbk).

Tratado de Medicina Paliativa y Tratamiento de Soporte en el Enfermo con Cáncer. M. G. Barón, A. Ordóñez, J. Feliú, P. Zamora y E. Espinosa. Editorial Médica Panamericana. 1996. ISBN 84 7903 223 5.

Palliative Care in the home. Doyle, D and Jeffrey, D. Oxford University Press, 2000. ISBN 0-19- 2632272 (Pbk).

Unipac one: the hospice/palliative medicine approach to end-of-life care. American Academy of Hospice and Palliative Medicine. 1998. ISBN 0-7872-5081-3.

(*)The versions in Spanish of the manual "Cuidando un enfermo en casa" and of the forms for the evaluation of symptoms and of psychological disorders, can be obtained free from the FEMEBA website at www.fermeba.org

19 Practical Tips for Health Care Professionals Planning to Teach in the Developing World

Eduardo Bruera, M.D.

INTRODUCTION

Modern palliative care started in the United Kingdom in the 1960's as a response to the unmet needs of patients with progressive incurable illness and their families. The original hospice movement in the United Kingdom emerged from independent community based programs and only after more than two decades of operation it started to be adopted by universities and major teaching institutions. The term "palliative care" and the adoption of palliative care by organized medicine and academic institutions took place initially in Canada and during the last decade it has become wide spread among the developed world. At the present time there are a number of undergraduate and graduate teaching programs in most countries and there are post-graduate training programs in medicine, nursing, and other health care disciplines.

Unfortunately, the development of both clinical and academic programs in the developing world is proceeding at a much slower pace. As a result, there are a very limited number of health care professionals with training and an even more limited number of clinical programs. This provides an opportunity for health care professionals from the developed world interested in transferring their knowledge and experience to help individuals and programs in the developing world become successful.

The purpose of this chapter is to provide some tips for health care professionals who are planning such visits. It is possible that by following these recommendations the visit will be more enjoyable and productive to both the visiting expert and the inviting local organizers.

BEFORE THE VISIT

The success of the visit depends overwhelmingly on the work done before the expert ever arrives. Most of the important questions that were not asked before the trip cannot be addressed once the expert has arrived. Therefore, it is important for planning to start several weeks before the planned visit. In most visits there are usually three parties involved: the expert visitor or group of visitors, the inviting local program or programs, and the funding source. In some cases the funding source is either the group of experts or the inviting organization. It is very important that all these parties become

actively involved in the main components of planning required before the visit. This chapter has been written from the perspective of the expert planning the visit. In this initial phase it is the expert's responsibility to actively involve both the inviting and funding parties.

Learning About the Place

Table 1 summarizes some important information the expert needs about the individuals, programs, and overall location where the visit will take place.

Table 1: Useful information about the local program	
1.	The structure of the health care system and reimbursement policies regarding palliative care
2.	Availability of palliative care services and medications, including potent opioids
3.	Model of care (inpatient, outpatient, home care, etc.)
4.	Administrative arrangements of the local program ("Top-Down" versus "Bottom Up")
5.	Patient population (Cancer, AIDS, etc.)
6.	Socioeconomic situation of the patients/families
7.	Communication style and cultural beliefs regarding diagnosis and prognosis

It is very important to appropriately understand the administrative arrangements of the local programs and individuals. Most programs in the developing world are "bottom up" programs. These programs range from stand-alone individuals or groups to small departments or clinical services within a community center of hospital. They have limited recognition by their peers and supervisors and have either limited or no mandate to provide palliative care. Their funding sources are not well defined and their ability to fund raise is frequently limited by the lack of independent administrative status. If the program you visit is a "bottom up" program it will be important to offer the local group the possibility of meetings with their immediate supervisors, the administrative authorities of the institution or local government where the care is being provided, representatives of the World Health Organization, etc. The expert needs to try to secure a formal mandate from organizations such as IAHPC or other national or international organizations in order to increase their credibility and be able to access some of those leaders. Considerable planning is required before the visit to ensure that all administrative leaders involved receive a consistent message.

Some local programs are "top down." These programs have a strong mandate from a major teaching institution, medical school, or regional or national health care service. Usually these programs are better established and funded. The main need from these programs is specific technical information about how to deliver care to patients and families. Patient based teaching, contact with local health care professionals, and small group teaching is very important for these programs.

Most programs will have some "top down" and "bottom up" components and they will need a combined approach to palliative care teaching.

It is very important to understand the type of patients seen by the local program. Some demographic and clinical issues will be very important for planning the education. Most palliative care programs in developed countries treat a majority of cancer patients. In the developing world other diseases such as AIDS, tuberculosis, malaria, and other not completely diagnosed chronic diseases can be a substantial proportion of the patient population. The relative proportion of local versus distant patients will dictate the need to deliver hands on follow up care versus providing education to local health care providers. The level of literacy will be very important in deciding assessment and educational tools. Some private institutions in developing countries treat patients a high socioeconomic status and the level of patient and family teaching in these centers is different from what is useful to the majority of the population who has a much lower socioeconomic status. For example, an international charity prepared and translated a large number of forms for self-assessment of symptoms and family education brochures. However, the patients and families treated by the local program had a literacy rate of 35%.

It is important to also understand the level of programs available in the center or community the expert will be visiting. For example, some centers have access to pain programs; others have access to psycho-oncology or volunteer visiting programs, etc. It may be possible to target the education to the level of existing programs and resources.

What Does the Local Palliative Care Program Have/Know?

The success of the visit will depend on its ability to build on top of current resources and achievements. Therefore, it is important to know the basic knowledge and resources so that the expert can avoid unnecessary repetition of already known material or discussion of agents and technologies that are just not available. For example, a number of experts visited programs in developing countries and conducted extensive education on the use of strong opioids such as morphine only to learn near the end of their visit that these opioids were largely not available in the country. It is very important to know in advance which opioids and other drugs are available and which of the drugs normally used by the expert are not available to the local program. Sending a list of drugs to the local organizers and asking them to submit a list of the available drugs to their program can easily address this. Technology available in the local area can range from state-of-the art to no electricity. Therefore, it is important to understand the availability of diagnostic and laboratory services, access to nurses and other health care professionals, etc. For example, during an educational visit to a 150 bed tertiary hospital I proposed a continuous subcutaneous infusion of morphine for a patient with ovarian cancer. This could not be implemented because there were only two infusion pumps available in the hospital and they were both being used for heparin infusion in the intensive care unit.

It is very important to know if the local program has received other expert visitors during the last year or two and the main subjects discussed by these individuals. One local program complained of the fact that over the course of one year they had received four visits by different experts who proceeded to address almost identical subjects to a very similar audience. Appropriate planning before each of those visits could easily have optimized this investment in time and effort.

Finally, it is always useful to ask if there are other programs in the region or the country that might benefit from this educational trip. The arrival of the expert might provide a wonderful opportunity for different programs in the country or region to get together and develop common approaches to the main palliative care clinical challenges.

Planning the Curriculum and Different Talks

A very useful approach is to set a series of very specific objectives for the visit. It is important that all parties agree to these objectives involved and that they be outlined as clearly as possible. For example, an objective such as "increasing physicians' knowledge on cancer pain" might be of limited impact. On the other hand, "understanding of the use of immediate-release opioids administered regularly by the oral and subcutaneous routes" provides a clear goal for some of the talks, clinical visits, and seminars. It also clarifies what will be necessary. In this example it will be necessary to have access to patients with cancer pain and also availability of oral and parenteral formulations of opioids. Once the set of specific objectives have been established, it becomes relatively easy to prepare a curriculum for the visit. The type of program ("bottom up" versus "top down") helps decide the number of planning and administrative meetings with government officers and administrators versus clinical teaching sessions.

It is very useful to have access to patients so as to demonstrate the different techniques for assessment and counseling. It is also very useful to have repeat visits with some patients over a number of days so as to demonstrate the response to different pharmacological and non-pharmacological interventions. It is important to have access to families to conduct family conferences and to demonstrate different counseling techniques. Finally, whenever possible it is very useful to conduct bus rounds in the community.

In some places it may be very useful to bring information on the preparation of different simple opioid solutions for oral, rectal, and parenteral administration. The help of a pharmacist in preparing this teaching material can be invaluable. When patients who are not able to take oral opioids or hydration the rectal and subcutaneous routes may be the only alternatives in most of the developing world.

Education needs to revolve around the drugs and diagnostic procedures that are readily available to local health care professionals. In one country widely disseminated information about cancer pain proposed a number of unavailable opioids and strongly discouraged the use of opioids such as meperidine and Buprenorphine. These two opioids are certainly not the most desirable for cancer pain but they happened to be the only ones available to this programs and health care professionals were hesitant to use them. A better planning of the teaching material would have prevented this conflict.

Teaching about counseling poses a particular challenge. In many countries patients are not informed about the diagnosis of cancer, and families assume responsibility for discussion with the health care team. Some of the cultural differences have been described in Chapter 2 of this publication. Other programs in developing countries apply full disclosure of diagnosis and prognosis to patients and families. Visiting experts need to plan their teaching understanding the limitations imposed by the local socioeconomic conditions and the influence of culture and religion in the daily life.

It is important to adapt the agenda to the local customs. For example, a well organized but rigid international lecturing program with a scheduled lunch break for noon in a country where lunch is usually served at 3:00 PM is inappropriate. Transportation can be extremely difficult in major urban centers in the developing world. Therefore, a very early starting time may result in lower attendance for the initial, and usually most crucial, sessions of the day. Table 2 summarizes some of the different educational tools available with the level of logistical components and the educational impact potential.

Table 2: Educational Tools for an Expert Visit

	LOGISTIC COMPLEXITY	EDUCATIONAL IMPACT
1. Plenary Lectures	↓	↓
2. Case Presentations	↑	↑
3. Patient Rounds	↑↑	↑↑↑
4. Bus Rounds	↑↑↑	↑↑↑
5. Workshops	↑	↑

THE VISIT

Many experts from developed countries will find that the standards of care are different from those they are used to with regard to medical assessments, availability of laboratory and diagnostic imaging, nursing support, drugs, and the overall physical plant of health care facilities. It is important to be prepared for these very significant changes and to avoid making negative comments about the overall system. The local palliative care group is unable to change the socioeconomic reality and the majority of the policies and procedures of the institution where they operate. The challenge for the expert is to help the local group in the process of inserting palliative care principles and practice into their local reality. Having a good understanding of existing standards will help the expert rapidly adapt the teaching to the clinical reality.

It is important to be very flexible in the delivery of the teaching components. It may become obvious that the local group has particular problems with an unexpected area such as communication, ethical issues, religious aspects or some issues of drug therapy. In that case it may be necessary to change the curriculum based on these findings. It is also important to remember that due to logistic and transportation difficulties educational sessions rarely begin (or end) on time. The most important educational sessions should take place late in the morning or very early in the afternoon since attendance is usually lower are the beginning and end of the day.

The ideal expert visit in palliative care should last not less than four to five days. It is very useful to have a nightly briefing session with the local organizers to discuss how things went during the day and propose changes for the next day. This briefing session may help address the level of satisfaction by the participants, the effectiveness of the translation services when those are required, necessary

meetings or discussions that have emerged from the day's events, and the scheduling of various possible interviews with local media.

The presence of the international expert provides the local organizers with a unique opportunity to highlight their program with the media. This helps educate patients and families, increases the visibility of the program with government officials, and can potentially attract donors. It is important for the expert to make him/herself available for multiple short interviews with the media and to take the opportunity not only to stress the importance of palliative care in general but also to emphasize the efforts made by the local group. Ideally, the members of the team of the local group should be invited by the expert to participate in the media interview.

AFTER THE VISIT

After returning home the expert should prepare a brief summary of the curriculum, the different findings, and the overall results of visit and send it to the local organizers and to the sponsor. Some of these summaries can be very interesting to readers of the main palliative care journals or the homepage of IAHPC. Many of these briefings provide excellent information about the experience of the expert that can be applied to many programs in addition to the one visited by the expert.

It is important to leave the local group with a series of very specific goals. It is also important to remain in contact with the local group on a regular basis to encourage them to reach the specific goals agreed to during the visit and to continue to provide support and encouragement over time.

CONCLUSIONS

There is great need for palliative care programs in the entire developing world. Health care professionals from the developed world can make an enormous difference for thousands of patients and families in those countries with a short visit of several days. It is important to spend considerable time planning appropriately the visit so that it will have the biggest educational, administrative, and social impact.

The visit can have profound beneficial effect on the visiting expert in addition to the obvious benefits to the local group. Expert visits frequently result in the establishment of long lasting relationships between teams in different areas of the world.

Suggested Readings:

Clark, D., Hockey F. and Ahmedzai, S. (eds.) Facing death: new themes in palliative care. Philadelphia: Open University Press, 1997.

Clark, D. The future for palliative care: issues of policy and practice. Philadelphia: Open University Press, 1996

Doyle D, Hanks GWC, MacDonald N. (eds.) Oxford Textbook of Palliative Medicine. Oxford University Press, 1997.

Barón M.G, Ordóñez A., Feliú J, Zamora P, Espinosa E. Tratado de Medicina Paliativa y Tratamiento de Soporte en el Enfermo con Cáncer. Editorial Médica Panamericana. 1996.

Doyle, D and Jeffrey, D. Palliative Care in the home. Oxford University Press, 2000.

American Academy of Hospice and Palliative Medicine. Unipac one: the hospice/palliative medicine approach to end-of-life care. 1998.

(*) The Spanish versions of the manual "Cuidando un enfermo en casa" and the Symptom and Psychological Disorders evaluation forms can be obtained free from the FEMEBA website at www.femeba.org

ANNEX 1 – WEB BASED RESOURCES

Compiled by: Derek Doyle, OBE, MD, FRCSE, FRCPE, FRCGP; Roger Woodruff, MBBS, FRACP, FAChPM; and Liliana De Lima, MHA

The following is a list of several web based resources available in the internet. IAHPC and the editors are unable to guarantee the quality, content and functionality of these tools, newsletters and/or links. When the URLs are not available, contact emails have been listed.

INTERNATIONAL AND REGIONAL ORGANIZATIONS

African Palliative Care Association
Email: apca@hospiceafrica.or.ug

Asia Pacific Hospice Network (APHN)
www.aphn.org

Cancer World
www.cancerworld.org

Children's Hospice International
http://www.chionline.org

Eastern and Central Europe Palliative Task Force (ECEPT)
http://free.med.pl/ecept/

Edmonton Regional Palliative Care Program
http://www.palliative.org/

European Association for Palliative Care (EAPC)
http://www.eapcnet.org/

Foundation for Hospices in Sub Saharan Africa (FHSSA)
http://www.fhssa.org/

International Association for Hospice and Palliative Care (IAHPC)
www.hospicecare.com

International Association for the Study of Pain (IASP)
http://www.iasp-pain.org/

International Association of Physicians in AIDS Care (IAPAC)
http://www.iapac.org

International Institute for the Advancement of Medicine (IIAM)
www.iiam.org

International Observatory on End of Life Care
www.eolc-observatory.net

Latin American Palliative Care Association - Asociación Latinoamericana de Cuidados Paliativos (ALCP)
Email: alcp@intercom.com.ar

MD Anderson Department of Palliative Care and Rehabilitation Medicine
http://www.mdanderson.org/departments/palliative/

Multinational Association for Supportive Care in Cancer (MASCC)
www.cancerworld.org/MASCC/default.asp

Open Society Institute
www.soros.org

Society for Integrative Oncology (SIO)
http://www.integrativeonc.com/

The Initiative for Pediatric Palliative Care
www.ippcweb.org

World Health Organization (WHO) Palliative Care Program
http://www.who.int/cancer/palliative/en/

World Health Organization Collaborating Center for Supportive Cancer Care
http://www.mdanderson.org/departments/CCSCC/

World Health Organization Collaborating Center in Policy and Communications in Cancer Care
www.medsch.wisc.edu/painpolicy

INTERNATIONAL PALLIATIVE CARE AND HOSPICE NEWSLETTERS

African Hospice Foundation News – (Free) Published by the Foundation for Hospices in Sub Saharan Africa
http://www.fhssa.org/newltr.html

American Academy of Hospice and Palliative Medicine Bulletin (Free)
http://www.aahpm.org/education/bulletin.html

American Society of Clinical Oncology (ASCO) News (Free)
http://www.asco.org/ac/1,1003,_12-002005,00.asp

Cancer Pain Release
Editor: Sophie Colleau, PhD
http://www.WHOcancerpain.wisc.edu/

Circular Asociación Latinoamericana de Cuidados Paliativos (In Spanish) (Free)
www.hospicecare.com/circular

Emanuel Hospice Newsletter. (Oradea, Romania) (Free)
To subscribe, please contact Ms. Kirsteen Cowling at hospice@casa.org.ro

End of Life/Palliative Education Resource Center
http://www.eperc.mcw.edu

European Association for Palliative Care (Free)
http://www.eapcnet.org/publications/news.asp

European Association for Palliative Care – East Newsletter (Free)
Editor: Sylvia Sauter Email: Sylvia.Sauter@stockholmssjukhem.se

Federazione Cure Palliative (In Italian) (Free - requires registration)
http://www.fedcp.org/newsletter.asp

Hong Kong Society of Palliative Medicine Newsletter (Free)
http://www.fmshk.com.hk/hkspm/newsletter/index.htm

Hospice Information Bulletin (Must become a member to receive bulletin)
http://www.hospiceinformation.info/publications/bulletin.asp
Indian Journal of Palliative Care (Free) (Contact Reena George to subscribe)
Email: reenamg@cmcvellore.ac.in

Initiative to Improve Palliative Care for African-Americans Newsletter (Free)
http://www.iipca.org/news.html

International Association for Hospice and Palliative Care (IAHPC) Newsletter (Free)
http://www.hospicecare.com/pubsindx.htm

International Association for the Study of Pain (IASP)
Pain: Clinical Updates (Free) (PDF File - Requires Acrobat Reader)
http://www.iasp-pain.org/PCUOpen.html

Innovations in End of Life Care (Free)
http://www2.edc.org/lastacts/

Kursbuch palliative care IFF- Palliative Care und Organisations Ethik (in German)
Editor: Anna Hostalek Email: pallorg.iff@univie.ac.at

National Hospice and Palliative Care Organization News Briefs (Free)
http://www.nhpco.org/i4a/pages/index.cfm?pageid=3640&openpage=3640

National Pain Education Council Journal to go (Free - Requires registration)
http://www.npecweb.org/journal.togo/journal.togo.asp

Newsletter Pediatric Palliative Care (Free)
http://www.hospicecare.com/journalpub/pediatric_palliative_july03.htm

Palliative Care Australia Newsletter (Free)
http://www.pallcare.org.au/newsletter/index.html

Palliative Care Council of South Australia Incorporated (Free)
http://www.pallcare.asn.au/newsltr.htm

Palliative Care Drugs Newsletter (Free - Requires Registration)
http://www.palliativedrugs.com/pdi.html

Partnership for Caring E-News (Free)
http://www.partnershipforcaring.org/WhatsNew/enews_set.html

Quality of Life Matters (by Quality of Life Publishing Co)
http://www.qolpublishing.com/prod1.html#qolm

Taiwan Hospice Headline (Free)
http://www.hospice.org.tw/english/news/right_news.asp

Texas Partnership for the End of Life Care (Free)
http://www.txpec.org/news/index.asp

The Palliative Platform (Free)
http://www.pccchealth.org/psmp/

EDUCATIONAL TOOLS AND RESOURCES

Achieving Balance in National Opioids Control Policy: Guidelines for Assessment
http://www.medsch.wisc.edu/painpolicy/publicat/00whoabi/00whoabi.htm

Agency for Health Care Policy and Research Clinical Practice Guidelines
Management of Cancer Pain
http://www.painresearch.utah.edu/cancerpain/guidelineF.html

Agency for Health Care Policy and Research Clinical Practice Guidelines
Manejo del Dolor por Cancer (In Spanish)
http://www.mywhatever.com/cifwriter/library/48/cpg2238.html

American Cancer Society Advanced Cancer and Palliative Care Guidelines
http://www.cancer.org

Bowel Obstructions: How to Recognize and How to Manage
http://www.palliative.org/PC/ClinicalInfo/NursesNotes/BowelObstructions.html

End of Life Care for Persons with Amyotrophic Lateral Sclerosis (ALS)
http://www.promotingexcellence.org/als/als_report/

End of Life Care for Persons with Mental Illness
http://www.promotingexcellence.org/mentalillness/

End of Life Nursing Education Consortium (ELNEC) Core Syllabus
http://www.aacn.nche.edu/elnec/index.htm

End of Life Palliative Care Education Resource Center (EPERC)
http://www.eperc.mcw.edu/

Finding our Way: Living with dying in America
http://itrs.scu.edu/fow/pages/FOWCOURSEINDEX.html

Hypermedia Assistant for Cancer Pain Management
http://www.painresearch.utah.edu/cancerpain/chtoc.html

IAHPC Palliative Care Manual
http://www.hospicecare.com/manual/IAHPCmanual.htm

Home Care Guide for Advanced Cancer
http://www.acponline.org/public/h_care/contents.htm

Managing Ascites in Palliative Care
http://www.palliative.org/PC/ClinicalInfo/NursesNotes/ManagingAscitesInPC.html

Manual para la Familia: Como Cuidar un Enfermo en Casa (In Spanish)
http://www.femeba.org.ar/paliativo/pacientes.html

National Pain Foundation Cancer Pain and Palliative Care Treatment Options
http://www.painconnection.org/MyEducation/TreatmentOptionsContinuum.asp?category=5

National Cancer Institute - Pain Control: A Guide for People with Cancer and their Families
http://www.cancer.gov/cancerinformation/paincontrolguide

Pediatric Palliative Care
http://www.promotingexcellence.org/childrens/index.html

Purdue Pharma Educational Resource Center
http://www.partnersagainstpain.com/index-mp.aspx?sid=2&aid=7819

Shaare Zedek Cancer Pain and Palliative Care Reference Database
http://www.chernydatabase.org

Spinal Cord Compression: A Palliative Care Emergency
http://www.palliative.org/PC/ClinicalInfo/NursesNotes/SpinalCordCompression.html

Supportive and Palliative Care for HIV/AIDS patients
http://hab.hrsa.gov/tools/palliative/

The Tri Central Palliative Care Program Tool Kit: Guide to Create an Outpatient Palliative Care Program
http://www.mywhatever.com/cifwriter/content/22/files/sorostoolkitfinal120902.doc

SYMPTOM ASSESSMENT AND RESEARCH TOOLS

After-Death Bereaved Family Interview
http://www.chcr.brown.edu/pcoc/toolkit.htm

Borg CR 10 Scale (Dyspnea assessment)
http://www.promotingexcellence.org/downloads/measures/borg_scale.pdf

Brief Fatigue Inventory
http://www.mdanderson.org/pdf/bfi.pdf

Brief Pain Inventory (long form)
http://www.mdanderson.org/pdf/bpilong.pdf

Brief Pain Inventory (short form)
http://www.mdanderson.org/pdf/bpisf.pdf

CAGE Questionnaire
http://www.mdanderson.org/pdf/cage.pdf

Caregiver Burden Scale
http://www.ku.edu/~kugeron/program/Appendix.pdf

Caregiver Strain Questionnaire
http://www.promotingexcellence.org/downloads/measures/caregiver_strain_questionaire.pdf

Edmonton Functional Assessment Tool (EFAT)
http://www.palliative.org/PC/ClinicalInfo/AssessmentTools/Efat.pdf

ECOG Performance Status
http://www.ecog.org/general/perf_stat.html

Edmonton Symptom Assessment System (ESAS)
http://www.palliative.org/PC/ClinicalInfo/AssessmentTools/esas.pdf

Edmonton Staging System
http://www.mdanderson.org/departments/palliative/display.cfm/?id=381E6C57-E6FB-11D4-810100508B603A14&method=displayFull&pn=B1C47163-DCCA-11D4-810100508B603A14

End of Life Chart Review - Administrative Information
http://www.gwu.edu/~cicd/toolkit/toolcharts.htm

FAMCARE Scale
http://www.promotingexcellence.org/downloads/measures/famcare.pdf

FAST - Stages of Alzheimer's disease
http://ec-online.net/Knowledge/articles/alzstages.html

Geriatric Depression Scale (In several languages)
http://www.stanford.edu/~yesavage/GDS.html

Grief Resolution Index
http://www.promotingexcellence.org/downloads/measures/grief_resolution_index.pdf

Hamilton Depression Rating Scale
http://www.members.optusnet.com.au/bill54/depresstest.htm

Herth Hope Index
http://www.promotingexcellence.org/downloads/measures/herth_hope_index.pdf

Karnofsky Performance Scale
http://www.acsu.buffalo.edu/~drstall/karnofsky.html

MD Anderson Symptom Assessment System
http://www.mdanderson.org/pdf/symptomassessment.pdf

McGill Quality of Life Questionnaire
http://www.promotingexcellence.org/downloads/measures/mcgill_qol.pdf

Missoula Demonstration Project Community Survey
http://www.promotingexcellence.org/downloads/measures/mdp_comm_survey.pdf

Memorial Symptom Assessment Scale
http://www.promotingexcellence.org/downloads/measures/memorial_symptom_assessment_scale.pdf Scoring:
http://www.promotingexcellence.org/downloads/measures/memorial_symptom_subscales.pdf

Mini Mental State Questionnaire
http://www.palliative.org/PC/ClinicalInfo/AssessmentTools/instruct%20for%20admin%20mmse.pdf

Palliative Outcomes Scale
http://www2.edc.org/lastacts/archives/archivesJan00/POSReg.asp

Palliative Performance Scale version 2 (PPSv2)
http://www.palliative.org/PC/ClinicalInfo/AssessmentTools/PPS.pdf

Partnership for Caring Advanced Directive Check List
http://www.partnershipforcaring.org/ToolKits/adchecklist.html

Pediatric Pain Profile
http://www.ppprofile.org.uk/

Quality of Care Check List
http://www.partnershipforcaring.org/ToolKits/qualitycarechecklist.html

Toolkit of Instruments to Measure End of Life Care - Patient Interview
http://www.gwu.edu/~cicd/toolkit/tool3.htm

Toolkit of Instruments to Measure End of Life Care - Surrogate After death Interview
http://www.gwu.edu/~cicd/toolkit/tool2.htm

Wong-Baker FACES Pain Rating Scale
http://www3.us.elsevierhealth.com/WOW/graphics/wong_faces.gif